THE American Journal OF Gastroenterology

VOL. 26, NO. 5 NOVEMBER, 1956

Chronic Cholangiolitic Hepatitis

Pancreatic Fat Necrosis

Medical Management of Benign Prolapse of the Gastric Mucosa into the Duodenum

Observations on the Development of Gastroenterology During Fifty Years

Twenty-second Annual Convention
Boston, Massachusetts
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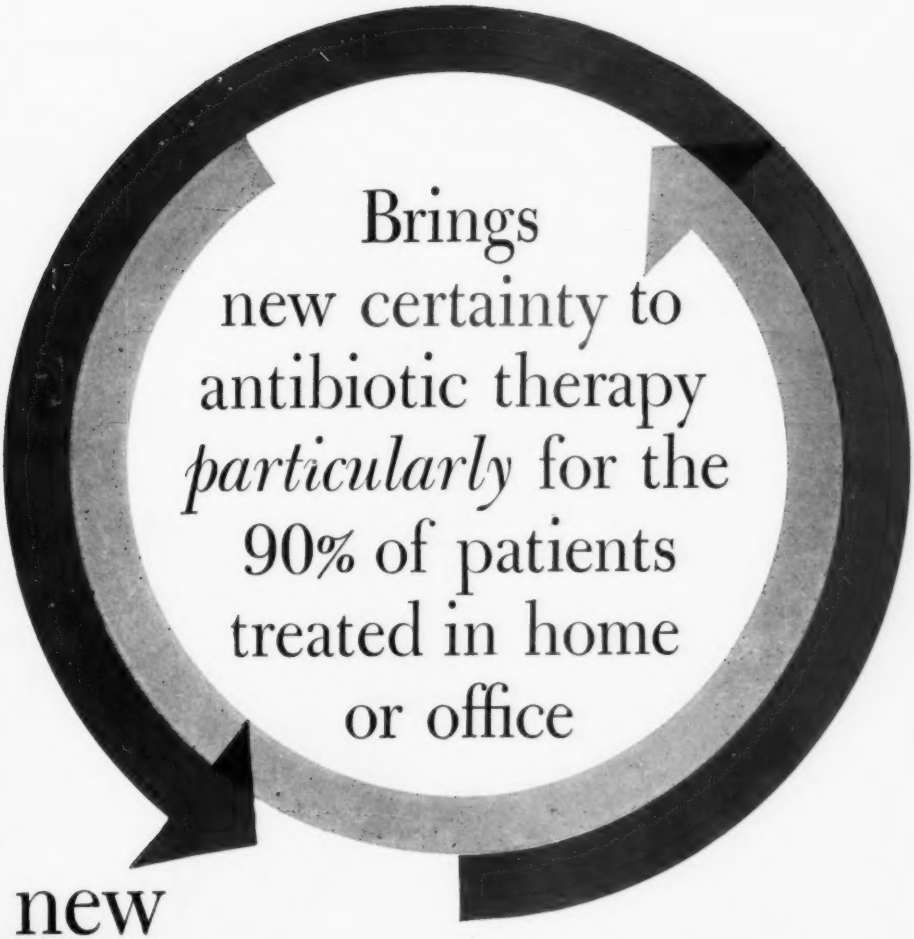
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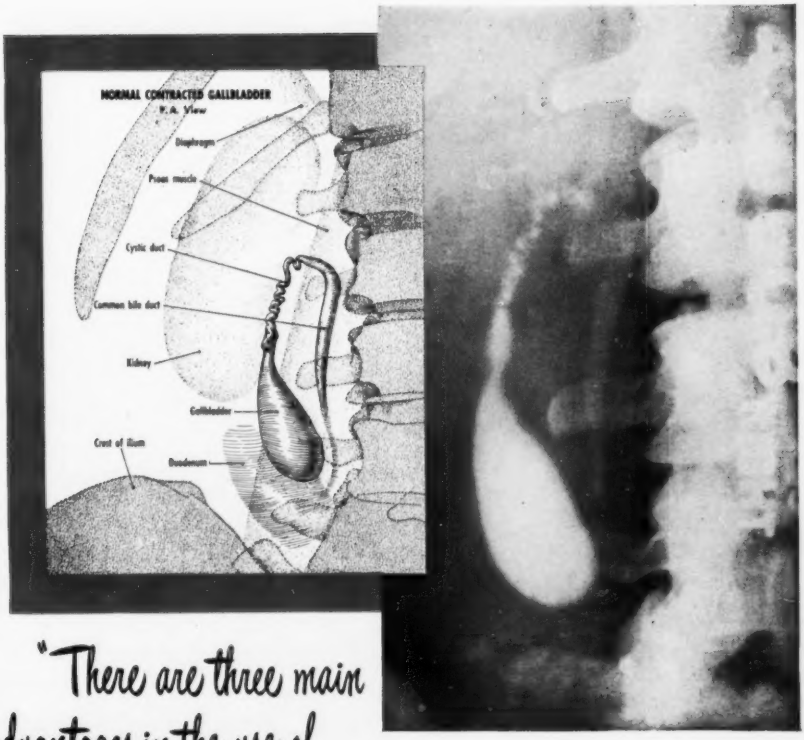
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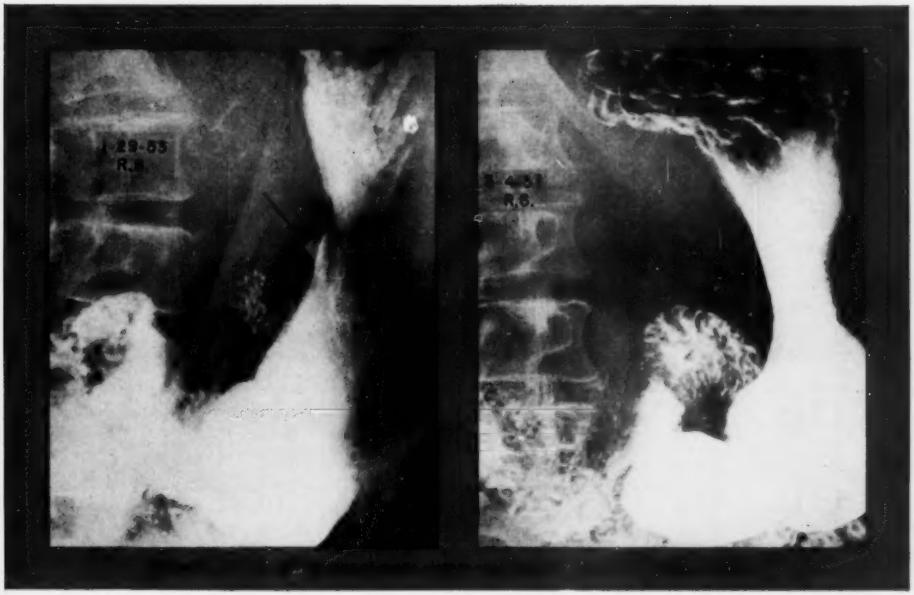
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CHRONIC CHOLANGIOLITIC HEPATITIS*

M. C. F. LINDERT, M.D., F.A.C.P.

Milwaukee, Wisc.

Numerous perplexities have arisen over the intrahepatic disease which has been designated by some as cholangiolitic hepatitis. The etiology, pathogenesis, and definitive treatment remain an enigma. The diagnosis and differential diagnosis is less obscure, particularly since the clinical features were so well described by Watson and Hoffbauer[1] just ten years ago. The diagnostic aspects of the condition are most troublesome during the *acute* phase; whereas, the therapeutic regimen becomes an extremely difficult and complex problem in the chronic stage. Except for general statements regarding this challenging liver disturbance, this presentation will be devoted to an analysis and evaluation of the treatment problems which arise during the course of chronic cholangiolitic hepatitis with development of cirrhosis. It is further hoped that a rational approach to the therapy can be evolved.

DEFINITION

The terminology of cholangiolitic hepatitis has not been uniformly accepted. Eppinger described a periacinar or cholangitis form of hepatitis. Watson and Hoffbauer[1] suggested the designation of cholangiolitic hepatitis. Lichtman[2] prefers the term *cholangiolotic* to that of *cholangiolitic*. Others have adhered to the inconsistent finding of inflammatory reaction in and about the cholangiolar system, which has resulted in the descriptive name of pericholangiolitis. As the result of these differences in opinions a number of synonomous designations have appeared in recent literature, especially for the chronic form of the disease. In this paper *chronic cholangiolitic hepatitis* is used to include those patients who have developed biliary cirrhosis and is considered as one of the types of primary biliary cirrhosis, thereby differentiating it from those forms of biliary cirrhosis in which there *is* obstruction or inflammation of extrahepatic biliary ductal system.

*Read before the Second Annual Convention of the American College of Gastroenterology, Chicago, Ill., 24, 25, 26 October 1955.

Etiology and Pathogenesis

There is no unanimity of opinion regarding these phases of the disease. A variable number of cases of sporadic or epidemic viral hepatitis have been observed to develop chronic cholangiolitic hepatitis. Lichtman[3] states that the viral determinant of this chronic form of hepatitis is entirely presumptive, since a similar picture has been produced in rats that have been fed ethionine. The clinical features at the onset, in addition to repetitious liver biopsy studies, is supportive evidence of the viral causation. We have seen cases in which repeated viral infection may ultimately result in the chronic form of this liver disease. LaManna[4] suggested a hematogenous infectious involvement of the small biliary radicles supposedly as a form of *descending* cholangiolitis or cholangitis. Hepatotoxic agents have been proven to produce a similar picture. Some of these hepatotoxins have produced an intrahepatic biliary obstruction, while others have produced jaundice by causing an increased permeability of the bile capillaries. On occasion a combination of etiological factors may be causative, e.g., viral and chronic alcoholic consumption. Alcoholic abuse plus other hepatotoxic agents may result in this picture.

In those patients with chronic disease presumably on a viral basis, the precise pathogenesis of the jaundice is still obscure. The aforementioned intrahepatic biliary obstruction and/or increased biliary capillary permeability have received consideration. In the absence of consistent histopathologic changes which might be considered diagnostic of cholangiolitic hepatitis, the mechanism of jaundice production remains open to speculation. In the far advanced cirrhosis due to cholangiolitic hepatitis the pathological picture may be difficult to differentiate from Laennec's cirrhosis or the hypertrophic biliary cirrhosis due to extrahepatic biliary obstructive lesions, which may terminate as an atrophic cirrhosis. Watson and Hoffbauer[1] emphasized two mechanisms by which the hypertrophic cirrhotic may become atrophic: 1. The large fatty liver loses fat and gains scar tissue. 2. The relatively nonfatty cholangiolitic cirrhotic later develops extensive fibrosis and shrinking. Invariably the end result is the same, unless reversibility can be instituted. The time interval from onset to advanced disease is extremely variable.

Diagnosis and Differential Diagnosis

Clinically, chronic cholangiolitic hepatitis should be suspected in patients with prolonged, moderately severe jaundice, two to four months in duration, with or without bouts of rather severe pruritus. Hepatic enlargement with splenomegaly is a consistent finding. The stools are light in color (acholic) and the urine dark (bilirubinuria). Zanthomatosis has been described but in our experience this has not been a common feature. Hyperpigmentation of the skin has been a marked and disturbing development in three patients, two female and one male. Lichtman[2] states that there is a delayed appearance of ascites and

pseudogallstone colic. Most of our patients have had nonascitic abdominal distention and an increase in the frequency and bulkiness of stools. Bone pain, particularly in the vertebral column, was a distressing symptom in a few cases. A flare-up and dissemination of psoriasis was observed in two patients. Easy fatigability, weakness, weight loss in spite of a reasonably good appetite has been the rule.

The laboratory studies are not diagnostic and mislead the clinician to serious consideration of an extrahepatic biliary obstructive lesion. Notably, hypercholesterolemia, elevated alkaline phosphatase, and a predominant increase in the prompt reacting serum bilirubin. These main features, in addition to normal turbidity or flocculation tests, normal or reduced urinary urobilinogen, normal prothrombin time, and normal total serum proteins would tend to rule out the liver parenchyma as the site of primary disease. These findings persist for months or years, until advanced cirrhosis ensues. As the disease progresses other laboratory changes are detected. Anemia is very apt to develop; it is usually a normochromic-normocytic type but at times hypochromic-normocytic. Ahrens et al[5] have reported the finding of soaps in the stools of 21 of 22 patients with primary biliary cirrhosis. Some of these patients were studied for pancreatic enzyme activity and all were found to be normal, thereby not responsible in those instances for the steatorrhea. Blood calcium and phosphorus studies were normal in several patients who exhibited steatorrhea with resultant bone changes consistent with osteomalacia.

In spite of a high index of suspicion and an excellent diagnostic acumen, a positive diagnosis of chronic cholangiolitic hepatitis cannot be made by the clinical and laboratory features just described. Serial liver biopsies have been of some assistance but pathognomonic histologic criteria are still wanting. As the lesion passes from the acute to the chronic phase, with cirrhotic changes more precise, pathological findings become apparent. Ricketts and Wissler[8] concluded that the process is primarily an inflammation in and around the smaller bile canaliculi, without evidence of parenchymatous liver disease. Finally, the only conclusive diagnostic measure is surgical exploration, with careful investigation of major biliary ductal system by direct visualization and cholangiography. This is the only means, to date, by which this lesion can be differentiated from any of the possible causes of an extrahepatic biliary obstruction, which is the clinician's principal concern.

Course and Prognosis

The rapidity of this disease is extremely unpredictable. There are undoubtedly many unknown factors which determine the course of this condition. Ricketts[6] has reported two cases with a short fatal course. The opposite extreme is cited by Watson and Hoffbauer[7], a case which extended over a period of 34 years from initial onset of probable cholangiolitic hepatitis to terminal cholangi-

olitic biliary cirrhosis. Ricketts and Wissler[8] published a most interesting case of a 27-year old female with a seven-year history of jaundice and pruritus, who spontaneously lost her jaundice and xanthomatosis following a bout of gastrointestinal bleeding due to ruptured esophageal varices. This same patient had an amelioration of the jaundice and hyperlipemia during a six-month period, apparently induced by a pregnancy of three months duration which terminated by miscarriage. Contrariwise, there are case reports in which pregnancy has produced intensification of jaundice and other associated symptoms. *In view* of these immoderations, the prognosis in any given case is almost impossible.

Therapeutic Considerations

Once the diagnosis has been established it is of importance that patient and physician alike realize they may very likely be dealing with a serious, protracted liver disease. This needs to be emphasized to the patient and family in order to accomplish full mental adjustment by the former and complete cooperation by the latter. The physician's attitude should be similar to that which he has toward chronic renal, cardiac or pulmonary diseases. A salient factor involved in the production of chronicity is probably that of the normal hepatocellular structure and function. The intrahepatic obstruction, *per se*, particularly when incomplete and not accompanied by infection, may be tolerated for a long time. The course becomes more rapidly progressive with increased obstruction, infection, and concomitant hepatocellular changes.

With these thoughts in mind, the therapy might be approached and divided in the following manner: Measures directed toward a) the liver, b) the symptomatic relief of distressing complaints, and c) the general systemic complications or sequelae.

Those measures which are directed toward the liver can be further subdivided into three parts, namely, the prevention of additional hepatic injury; the promotion of hepatic healing (cholangiolar); the stimulation and/or maintenance of biliary flow. The prevention of superimposed hepatic injury encompasses most of the principles involved in the treatment of any diffuse hepatic disease, such as viral hepatitis or portal cirrhosis. The patient is to avoid alcoholic abuse and exposure to chemical or drug hepatotoxins. Foci of infection or concomitant systemic infections should be eradicated, if feasible. The most useful group of medications to accomplish this has been the antibiotics. They have also been tremendously beneficial in the management of complicating infections. Prolonged shock or anesthesia should be avoided to avert hepatic anoxia. Elective traumatic surgery is to be postponed or permanently avoided, if possible. The patient is cautioned about prolonged exposure or exhaustion. Prophylactic measures are probably indicated to prevent pregnancy. Concomitant chronic illness of another system, e.g., cardiorenal or pulmonary disease, should be treated energetically. Transfusions of whole blood should only be

given on strict indication and plasma infusions should be used as a last resort for replacement therapy. Blood donation is contraindicated, in spite of adequate blood counts, to avert the stress factor or anoxia. So-called minor surgical procedures are to be performed with the same diligent precautions as major procedures. Minor illnesses, e.g., upper respiratory infections, require early and vigorous therapy. The fundamental principles which are utilized to promote healing of primary hepatocellular injury are applicable to that of cholangiolitic disease. Bed rest, which is such a vital part of the treatment in most types of active liver disease, is also a salient feature of chronic cholangiolitic disease therapy but in modified degree. Complete bed rest is not rational nor has it appeared particularly beneficial. Daily rest period and adequate rest at night seems indicated and helpful. The total amount of rest in these cases should be individualized, depending upon the effect of activity upon the serum bilirubin level and the existence of concomitant disease conditions, e.g., heart disease. *Diet* plays an important role in the healing of liver diseases. Whether it is as important in the absence of hepatocellular injury is debatable. Nevertheless, it becomes a greater necessity as the disease progresses. The usual hepatic diet, high carbohydrate (350-500 gm.), moderate protein (100-120 gm.), and moderate fat (50-80 gm.), is generally utilized. Lower fat diets have been tried in those cases with marked hypercholesterolemia and xanthomatosis or psoriasis. The administration of reduced fat diets often sacrifices the palatability of the entire feeding. At times it is most desirable to permit a self-selected diet. Dietary supplements, such as lipotropic agent and vitamins, are given empirically. Calcium intake, by means of food or medication, is indicated in those patients with steatorrhea or those who have bone pain with the demonstrable evidences of osteoporosis or osteomalacia. The intermittent use of the broad spectra antibiotics appears to have controlled the process or hastened healing. It is apparent that such an effect would be difficult to prove. It is my personal feeling, however, and observation that these patients do better when this procedure is followed. This is probably accomplished in several ways: control of intrahepatic infection, reduction of intestinal bacterial flora, suppression or elimination of hidden foci of infection, and finally, by a possible nutritive factor or factors in the antibiotic itself. Continuous use of these antibiotics may be hazardous. Seven to 14 day intervals every month or two have been without danger. Alternation of antibiotics has also seemed worthy of further trial. This manner of antibiotic exhibition is certainly warranted when one considers the parallel of extrahepatic cholangitis with intrahepatic cholangiolitis. Attempts at stimulating or maintaining bile flow should theoretically improve this hepatic lesion. Such an approach would be more rational if the pathogenetic mechanism was purely obstructive. Watson and Hoffbauer[7] stated as follows in Case 6: "No benefit was derived from the surgical exploration and the external biliary drainage insofar as the patient was concerned." Further in their Case 7 they noted that drainage of the gallbladder failed to influence the jaundice or pruritus. These authors and others also reported on medical stimu-

lation, using oral bile salts and intravenous Decholin. Neither mode of administration influenced the biliary flow. Despite these discouraging experiences, we have continued a combined medical-surgical attempt to increase or release bile flow. Since the majority of patients come to surgical exploration, we have advised prolonged drainage by T-tube for as long as a year. In this way one can be more certain of continuous extrahepatic duct patency. Several of our patients who succumbed were found at autopsy to have extremely small, atrophic (?) extrahepatic ducts, whereas at previous surgical exploration they had normal-sized biliary ducts. Further, it is conceivable that accumulations of debris, with high cholesterol content, may add to the delay in bile flow. Repeated irrigations of the T-tube and extrahepatic ducts may assist in insuring their patency. Simultaneous with this surgical approach one may institute a biliary flush regimen, using atropine for antispasmodic effect and magnesium sulfate, bile salts or fatty feedings for cholagogue or cholerectic effect. It is believed that this combined method, when instituted early, may ultimately prove to be a therapeutic adjunct.

The symptomatic treatment eventually becomes a major part of care of these cases. One of the most distressing symptoms is that of severe, usually generalized, pruritus. Numerous widely known medications for internal and external administration have been used. Poor results have been obtained when using ergotamine preparations, external lotions, and methyl testosterone. It must be remembered that the latter has been shown to be hepatotoxic. Antihistaminics have been transiently effectual. The antihistamine of choice is determined by trial and error. Combinations of mild sedation with salicylates has been helpful in some instances. Nicotinic acid has aggravated the itching. One patient obtained temporary daily relief by scraping her skin with a knife or razor blade. Jaundice, next to pruritus, is a most disturbing symptom. Careful explanation and reassurance is necessary for proper patient adjustment. It should be clearly understood that the pigmentation, *per se*, does not determine the severity or prognosis of the illness. Back pain, especially of the radicular character, can be a difficult problem. Ahrens et al[5] described 7 of 22 patients who developed severe back pain within one to ten years after the onset of primary biliary cirrhosis. They concluded that osteoporosis was the cause of compression changes in the vertebral column and was probably due to at least two factors: 1. Faulty fat absorption with avitaminosis-D and with calcium lack due to formation of insoluble calcium soaps in the intestine, and 2. inadequate formation of bone matrix as in Albright's postmenopausal osteoporosis. In the absence of the latter factor, the situation may be correctly designated as osteomalacia rather than osteoporosis. Treatment of this symptom necessitates increased calcium and Vitamin D intake, nerve blocks, corrective corsets or body casts. Back pain may resolve in the absence of demonstrable recalcification of the bone. The appearance of ascites and edema is a disturbing and at times distressing symptom. It is managed in the same manner in this liver lesion as in

other types of liver disease. Low salt intake, diuretics, and protein replacement are the principal measures employed. As stated earlier in this report, fluid accumulations may be a relatively late development.

Finally, there are certain measures directed toward general systemic complications or sequelae of this unusual form of liver disease. Invariably, as the process goes on, hematological changes are noted. The most frequently noted alteration is that of a normochromic-normocytic anemia or a hypochromic-normocytic anemia. Iron therapy is indicated but may not improve the blood picture. Vitamin B_{12} and liver extracts have also been used without dramatic result. All should be given a prolonged therapeutic trial. Transfusions are not without hazard and should accordingly be avoided and used only with strict indications. Gastrointestinal disturbances may be multiple and vague. Bloating, belching, excessive gas, anorexia, and bowel habit changes all require attention. Ahrens et al[5] observed "deficiency patterns in 10 of 15 patients with primary biliary cirrhosis". Bile salts, pancreatic extracts, vitamins, calcium—all may aid in alleviation of these complaints. In addition to the previously mentioned pruritus there are other dermatological changes which indicate special attention. These include skin infections secondary to scratching, xanthomatosis, psoriasis, and marked hyperpigmentation. Avoidance of prolonged and excessive exposure to the sun or ultraviolet may modify the latter. Low fat diets and special ointments assist in control of the xanthomatosis and psoriasis. Mildly antiseptic skin ointments and meticulous cleanliness control the secondary skin infections. Skeletal changes, such as osteoporosis and osteomalacia resulting in radicular pains, have already been mentioned. Other systems may be involved but in lesser degree or in an unknown manner. For example, the endocrine system may very probably be implicated since a greater number of females develop chronic cholangiolitic cirrhosis than males. This aspect has been difficult to evaluate and investigative studies have been inconclusive.

Summary

Chronic cholangiolitic hepatitis is a difficult disease to diagnose and treat. An attempt has been made to evolve a therapeutic approach whereby the treatment measures be directed toward the liver, the troublesome symptoms and the complications and sequelae. The results to date indicate that the regimen is worthy of trial but not too encouraging.

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PANCREATIC FAT NECROSIS*

V. Attempts at Therapy

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In previous work we have employed different substances in the prevention of experimental fat necrosis in the dog[1,4]. The latter was produced by excision of the pancreatic duct together with a piece of duodenum and leaving the duct open (after the duodenal defect was closed), so that activated pancreatic secretion would drain freely into the abdominal cavity.

The best results in the prevention of fat necrosis had been obtained with 2 lipase inhibitors, sodium formaldehyde sulfoxylate (SFS) and quinine. These substances decreased the occurrence of fat necrosis from 85 to 38.5 per cent and mortality from 80 to 31 per cent. In continuation of this work, we tried several other substances and combinations of them for their prophylactic effect on fat necrosis.

Methods

Fifty-four healthy mongrel dogs of either sex (9–12 kg. weight) were used for these experiments, which were performed as described in our previous publications[5,6].

Results

Table I shows the substances used and the results obtained.

Since SFS, as well as quinine, has been found quite effective in preventing pancreatic fat necrosis, we tried a combination of both substances (Experiment 1). This, however, proved less effective than the single substances, due possibly to the fact that the mixture of the two chemicals causes a chemical reaction between them.

Diamox† in doses up to 55 mg./kg. had given negative results in previous studies[4]. Since Dreiling and his associates have shown[7] that a maximum effect

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†Diamox® was kindly supplied by Dr. J. M. Ruegsegger of Lederle Laboratories.

of Diamox is attained with doses of 50 mg./kg. and more, we gave 100 and 200 mg./kg., but even these amounts showed no beneficial effects (Experiment 2–3). The experiments with pyribenzamine (Experiment 4) were performed on the assumption that administration of antihistamines might lessen the toxic effects of the fat necrosis; however, the results were negative. The combination of SFS with pyribenzamine did not produce an improvement over the results obtained with SFS alone (Experiment 5).

TABLE I

Exper. No.	No. of Dogs	Administration of Drugs		Results in %	
		Intraabdominal at Operation	Intrav., Subcut., or Intramusc.	Fat Necrosis	Fatal
1	4	2g. SFS**–1g. quinine sulfate		75	50
2	4		Diamox i.v. 100 mg. p. kg.*	100	71
3	3		Diamox i.v. 200 mg. p. kg.*		
4	8		Pyribenzamine s.c. 25 mg.*	75	63
5	3	2g. SFS	Idem	100	33
6	4	Methenamine 100 mg. p. kg.	Methenamine 100 mg. p. kg. i.v.*		
7	4	Methenamine mandelate 100 mg. p. kg.	Methenamine mandelate 100 mg. p. kg.*	75-100	50-75
8	4		Sodium formaldehyde bisulfite 100 mg. p. kg. i.v.*		
9	4		Sodium sulfoxylate 100 mg. p. kg. i.v.*		
10	6		Pro-Banthine 12.5 mg. i.m. 3 times daily	83	66
11	10	5g. SFS	Idem	50	30

*Twice daily.

**Sodium formaldehyde sulfoxylate.

Various substances which were chemically related to SFS, like the formaldehyde containing compounds, methenamine, methenamine mandelate†, sodium formaldehyde bisulfite, and sodium sulfoxylate (which is SFS without formaldehyde), proved to be failures (Experiments 6–9).

†Methenamine mandelate was furnished through the courtesy of Dr. G. W. Mast, Nepera Chemical Co.

Finally, Pro-Banthine‡ alone and the combination of SFS with Pro-Banthine was tried (Experiments 10, 11). Pro-Banthine alone did not prevent fat necrosis and did not lower the mortality appreciably, but it was thought that the inhibition of gastric and pancreatic secretion by Pro-Banthine might add to the beneficial effects of SFS. This combination, however, did not fulfill our expectations. The mortality from fat necrosis was approximately the same as with SFS alone (30 per cent and 31.5 per cent respectively), and the occurrence of fat necrosis was higher (50 per cent and 38 per cent).

Conclusions

1. Our attempts to improve the results of our previously reported experiments on the prevention of pancreatic fat necrosis were unsuccessful.

2. The combination of sodium formaldehyde sulfoxylate (SFS) and quinine, the use of substances chemically related to SFS, Diamox in higher doses, antihistamines with or without the addition of SFS, proved unsuccessful. The combination of SFS with Pro-Banthine gave results which were about the same as with SFS alone.

3. Under the conditions of our experiments, the intraperitoneal application of SFS or of quinine sulfate are so far the best means to reduce the occurrence and the mortality from experimental pancreatic fat necrosis.

Summary

In studies on the prevention of experimental pancreatic fat necrosis, no procedure has been found which is superior to the intraperitoneal application of sodium formaldehyde sulfoxylate or of quinine.

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FURTHER STUDIES ON CHOLESTEROSIS OF THE GALLBLADDER

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Although cholesterosis of the gallbladder (strawberry gallbladder) is a common finding among autopsy and surgical material, there is an impelling need for further investigation of the etiologic factors which produce this condition. Cholesterosis of the gallbladder has been described in textbooks and in the literature under the titles of strawberry gallbladder, chronic cholecystitis and lipoid cholecystitis. The autopsy incidence of cholesterosis of the gallbladder range from 12.5 per cent[12] to 36.8 and 38.5 per cent[9-15]. The surgical incidence range from 8.8 per cent[14] to 39 per cent[16].

In a previous study we reported an autopsy investigation of 165 cases of cholesterosis of the gallbladder[12]. It is the purpose of this communication to clarify the varying opinions regarding the etiology of cholesterosis of the gallbladder, with further appraisal of the pertinent data, and to report our findings in 35 surgical cases. Of the 35 surgical cases, 18 revealed a diffuse cholesterosis, and 17 a cholesterolatomatous papilloma.

Association of Cholecystitis with Cholesterosis

It has been believed that cholecystitis is commonly associated with cholesterosis of the gallbladder and is an etiologic factor in the production of this condition. Our autopsied cases revealed little or no evidence of inflammatory changes associated with cholesterosis, which apparently indicated that inflammation played but a minor role in the production of this condition. We have noted that in most of our autopsied cases which presented evidence of cholecystitis, it was associated with gallstones. Many authorities[1] have likewise observed the existence of inflammatory changes, when it was associated with gallstones. It has been stated that cholesterosis of the gallbladder is essentially an asceptic process[15]. Bacterial studies of material secured from the gallbladder with cholesterosis have shown little evidence of infection, the majority of specimens have proved to be sterile[13]. In our autopsy studies we reported the occurrence of chronic cholecystitis in only 14.5 per cent of cases. In 368 autopsied cases of cholesterosis reported by Crump[9], there were 165 without any associated pathology.

In the present study of 35 surgical cases of cholesterosis of the gallbladder, cholecystitis was found in 16 or in almost half of the cases. This incidence of inflammatory changes exceeds those observed among our autopsied cases. The reason why the surgical cases show a greater incidence of cholecystitis, is no doubt due to the presence of gallstones and gallbladder symptomatology which necessitated surgical intervention.

Association of Gallstones with Cholesterosis

It has been believed that gallstones is a common accompaniment with cholesterosis of the gallbladder. Our autopsy studies had shown that gallstones occurred in only 10.9 per cent of cases[12]. In 368 autopsied cases of cholesterosis, Crump[9] found 30 cases with gallstones, an incidence of 8.1 per cent. Furthermore, our autopsy study had shown that gallstones were not usually associated with cholesterosis of the gallbladder, unless there was an associated cholecystitis. Of 24 cases with cholecystitis, 16 presented evidence of gallstones and in 8 instances of cholesterosis it occurred without stones.

Of the 35 surgical cases of cholesterosis of the gallbladder, 16 presented evidence of cholecystitis, and of these 15 revealed gallstones. Even in the surgical cases the presence of gallstones was only noted in those which showed evidence of a cholecystitis. The high incidence of gallstones observed in surgical cases had led to the assumption that stones were a common finding associated with cholesterosis of the gallbladder, notwithstanding the fact that the surgical cases were those selected for operation because of gallbladder symptomatology.

Age:—In the 35 surgical cases, 21 or 60 per cent occurred between the 4th and 6th decades. This age period coincides with our autopsy cases which likewise revealed a similar prevalence among the older age group. In Crump's[9] 368 autopsied cases, 316 occurred beyond the age of 30, and of these, 219 were between the 5th and 7th decades.

Sex:—Of the 35 surgical cases of cholesterosis of the gallbladder, there were 5 men and 30 women. Obviously, there is a marked difference of sex incidence between the autopsied and surgical cases. In the autopsied cases the condition occurred more frequently in males, while in the surgical cases it is more prevalent in females. This difference of sex incidence is in accord with other statistical data which had shown a greater preponderance of females in surgical cases.

Roentgen examination:—There is a wide divergence of opinion regarding the roentgen findings in cholesterosis of the gallbladder. The lack of unanimity among roentgenologists is understandable, but this is no doubt the result of variable roentgen changes observed in the cholecystographic examination of this condition. Many authorities believed that the strawberry gallbladder commonly produce an abnormal cholecystographic picture, while others are of the opinion that the condition more commonly shows a normal functioning gallbladder. Although there is conclusive evidence that cholesterosis of the gallbladder may portray a shadow of normal dye density and a normal appearing vesicle shadow, this is dependent upon the degree of pathologic involvement and the presence of associated conditions, such as cholecystitis and/or gallstones. Some authorities believed that the gallbladder tends to empty too rapidly or that it empties too slowly, while others have observed changes in contour and density of the cholecystogram. There is no question that the above findings may occur in many instances. However, it must be emphasized that

these changes are dependent upon the presence of cholecystitis and/or gallstones, and are not usually observed in the uncomplicated case of cholesterosis of the gallbladder.

Pathophysiology:—The mechanism in which cholesterol is deposited within the gallbladder mucosa has not been satisfactorily explained. Bagnoli and Monaci[4] believed it to be caused by an abnormality of absorption of intramural lipids resulting from venous and lymphatic stasis of the gallbladder. Rolleston and McNee[22] also state that lymphatic obstruction results in the villi becoming loaded with cholesterol absorbed from the gallbladder bile. On the other hand, Pezzuoli[19] who was able to experimentally produce lipoidosis of the gallbladder in the chick by administering a very high dosage of diethylstilbestrol, concluded that lipoidosis of the gallbladder mucosa is not derived from the absorption of cholesterol contained in the bile. His findings indicate that the cholesterol deposition in the gallbladder mucosa must then be produced from extrabiliary sources, presumably from the blood plasma. It has been recently shown, however, by Byers and Friedman[8] that there is no relationship between biliary cholesterol concentration and blood plasma cholesterol.

There is considerable evidence to indicate that cholesterosis of the gallbladder is not an inflammatory condition, though some authorities believe that inflammatory changes occur in this condition at some time during the development of the cholesterosis gallbladder. The pathophysiology of cholesterosis is generally thought to be the result of localized disturbance of cholesterol absorption from the bile. While there seems to be no unanimity of opinion regarding the pathophysiology of absorption and excretion of cholesterol and lipids within the gallbladder, it is nevertheless believed that the cholesterol deposition in this condition is either derived from the bile, which is absorbed by the mucous membrane of the gallbladder[7,23,13,15], or to secretory changes of the mucosa resulting from an inflammatory process[10,11]. Biliary stasis was thought to have been an etiologic factor in the production of cholesterosis, but this is held to be unlikely, since in the absence of cholecystitis and/or gallstones, the gallbladder is often roentgenologically shown to function normally.

Effect of Changes in the Cystic Duct in Relation to Cholesterosis of the Gallbladder

It has been noted that in the strawberry gallbladder, duodenal drainage yielded evidence indicative of an hypertrophy of the sphincter of Oddi, and that the resulting biliary dyskinesia was thought to be a causative factor in the production of cholesterosis[18,5]. In a study of 10 cases of noncalculus strawberry gallbladders, Almasque Dedue and Braier[3] employed the combined methods of duodenal drainage, operative cholangiography and cholangiomanometry, found the cystic duct to be involved in 5 of the cases as a result of dyskinesia. Albot and his coworkers[2] made radiomanometric and pathologic determinations of the biliary tract, arrived at the conclusion that a subacute inflammatory

process of the cystic duct was the primary lesion in cholesterosis of the gallbladder. They were of the opinion that the cysticitis was responsible for the parietal lipoidosis resulting in a high cholesterol concentration in the bile and a parietal lymphatic stasis.

There seems to be some pathologic basis in the belief that changes in the cystic duct and the neck of the gallbladder may possibly play an important role in the production of cholesterosis of the gallbladder. In cholesterosis of the gallbladder, Roberts[20] has shown on microscopic examination that the lipoid material in the mucosa is primarily confined to the prominency of the mucosal ridges, which when traced toward the neck of the gallbladder, are usually found to end at the junction of the vesicle and the cystic duct. Since it has been observed that the neck of the gallbladder and the proximal cystic duct is involved in the pathology of cholesterosis, it may be important to further investigate these segments for a more detailed histopathologic study. It is quite possible that there may be some histopathologic changes occurring within the glandular structure of the mucosa which may play an important role in the etiology of cholesterosis. The possibility of a causal relationship of mucosal glandular dysfunction of Rokitansky-Aschoff sinuses or Luschka's crypts and cholesterosis has not been explored. These crypts are commonly noted in gallbladders beyond the age of 30[21], during the age period in which most cases of cholesterosis occur. Moreover, it has been shown that these crypts are more numerous in the neck area of the gallbladder[6]. It is not then an unreasonable deduction to suppose that there may be a possibility that the Rokitansky-Aschoff sinuses may be involved in cholesterosis of the gallbladder. This phase of the problem of the anatomic and histopathologic changes in the etiology of cholesterosis needs to be more fully investigated.

Summary

A comparative study of the relative surgical and autopsy incidence of cholesterosis of the gallbladder has been made. The reason why the surgical incidence of cholecystitis and gallstones are greater, is due to the fact that they were selected cases which presented a gallbladder symptomatology requiring surgical intervention. The variable roentgen findings observed in cholesterosis of the gallbladder is dependent upon the degree of the associated cholecystitis and the presence of gallstones. The etiologic factors involved in the causation of cholesterosis of the gallbladder and the pathophysiologic mechanisms are described. The possible relationship of dyskinesia and inflammatory changes in the cystic duct and neck of the gallbladder as causative factors in the etiology of cholesterosis are discussed. Consideration should be given to dysfunction of the mucosal glands of the crypts of the gallbladder in order to determine whether any relationship exists between them and cholesterosis. The problem of the physiologic mechanisms involved in lipid absorption and secretion by the gallbladder mucosa has scarcely been explored and awaits further investigation.

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NORMAL BODY HAIR AND PORTAL CIRRHOSIS

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Spellberg states that pectoral alopecia may precede and aid in establishing the diagnosis of portal cirrhosis. To our knowledge, however, inadequate evidence exists to support the common clinical assumption that a sparsity or actual loss of body hair coexists with cirrhosis. We wish to present clinical observations which favor the opposite view that the amount of body hair should not be regarded as of diagnostic significance in portal cirrhosis.

TABLE I

OBSERVED BODY HAIR MASS IN PATIENTS WITH AND WITHOUT CIRRHOSIS

Group	Heavy		Moderate		Sparse		None		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
Cirrhosis	3	8	13	33	22	55	2	4	40	100
Alcoholics	1	8	2	16	10	76	—	—	13	100
Other Diseases	6	12	20	40	23	46	1	2	50	100

METHODS

During the six-month period from March to August 1954, 103 patients at the Los Angeles County Hospital were carefully interviewed and examined. These patients were divided into three groups: 40 with portal cirrhosis; 50 with other diseases; and 13 with chronic alcoholism. Clinical evidence of diseases of endocrine origin was absent.

Detailed inquiries were made to establish any change the patient or his acquaintances had observed in the amount or growth of his body hair, particularly of the pectoral and axillary areas.

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Examination by direct inspection was specifically made to appraise the presence of either markedly heavy or scant hair growth.

The duration of known cirrhosis in these patients was from one month to 12 years. Thirty exceeded one year. All 40 had imbibed alcohol daily for 2 to 35 years, and 35 of these drank whiskey. The chronic alcoholic patients without cirrhosis professed daily alcoholic intakes ranging from 1 to 81 years, and ten drank whiskey.

Results

One hundred of the total of 103 patients declared there had been no change in body hair growth or mass since puberty. Two of three patients with cirrhosis had experienced a slight increase of their pectoral hair. A third shaved less often.

The distribution of body hair mass is shown in the table. Allowing for the limitations of making a sharp division between the moderate and sparse groups, there is not significant preponderance of cirrhotics with scant hair mass. Those with frank pectoral and axillary alopecia were so few in number as to preclude statistical significance. Most of the group of chronic alcoholics without cirrhosis had scant body hair.

Comment

These observations suggest that the amount of body hair mass cannot be regarded as of diagnostic significance in evaluating a patient with suspected portal cirrhosis. Scant body hair occurs with about the same frequency in patients with other diseases in the same hospital population.

Although most of the chronic alcoholics without cirrhosis have scant body hair, the group is too small to evaluate. It is more significant that the amount of body hair of the cirrhotic patients, all of whom drank alcohol daily, is essentially the same as in the control group.

Conclusion

Patients with portal cirrhosis experienced no loss of body hair and had about the same mass of hair as did patients in the control group who had other diseases. Hence, a body hair pattern of diagnostic significance is not associated with portal cirrhosis.

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THE GALLSTONE—SILENT, GROWLING OR SCREECHING

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In the past we have believed that infection was the primary source of trouble in the biliary system; some of us were even hoodwinked by the theory that this infection could be secondary to appendicitis or even tonsillitis. But now we believe that the gallstone is the culprit which does the immediate damage, and that its forebears are metabolic changes in the bile, with excess cholesterol, and trouble with filling and emptying of the extrahepatic biliary system leading to stasis. Though the stone may have more or less innocent beginnings, when mature it may become destructive. It may be equally destructive though minute or immense, from 2 mm. to 5 cm. As long as it floats around in the gallbladder, it is innocuous, but when it gets restless and discontented with its dull habitat, and starts moving out, it changes into an instrument of terror.

We use the term "silent" gallstone, meaning by that a stone resting serenely in the biliary vesicle and allowing the host and the host's physician to sleep peacefully. If it begins to rub its shoulders against the walls of its abode, its host becomes aware of a disturbance which might be termed a growl; especially if it explores for a means of exit.

The host's physician may counsel, "Though your gallstone growls a little, for the most part it is 'silent'. 'Let the sleeping dog lie' ".

But the physician has missed the proper figure. This apparently innocent little member is not what he may seem to be. We will do better to think of it as a sly feline, ever alert, and ready to pounce; and when it does it will be a snarling, screeching wildcat, intent on tearing its victim to pieces.

Why is the gallstone "silent"; why does it "growl"; why does it "screech"? So far in this exposition, this gallstone has been an animated lump of cholesterol or calcium which may become a menacing ogre. This for purposes of emphasis. Now we must admit that its role is passive; it simply goes where it is pushed. But we must still maintain that the effects are just as terrific and destructive.

In order to understand how this little devil operates; or why this "silent" little clod is forced to become a demon, we must understand a few simple facts of anatomy and physiology of the biliary system.

The gallbladder and its outlet are like a funnel, albeit a crooked one, tapering, with valves in its narrow outlet. Whenever the owner eats any food containing fat, the gallbladder contracts vigorously and exerts a pressure on its contents. This tends to push any stone large or small into the narrows of the funnel. Very small stones may pass into the cystic duct and even into the com-

mon duct; a larger stone may become blocked in the ampulla of the gallbladder. Whichever way it is, the pressure of the stone produces pain by irritation of the nerves in and around the passageway, and provokes reflex disturbances such as vomiting. Blockage of the ampulla of Vater by a stone will produce jaundice, liver damage by pressure, and possibly cholangitis. Now we believe that blockage here may interfere with the emptying of the pancreatic duct resulting in varying degrees of pancreatitis. A stone impacted in the outlet of the gallbladder interferes with the return circulation and also prevents evacuation of its contents, resulting in distention, swelling, inflammation, and often gangrene and perforation.

Further evidence that these phenomena are obstructive primarily is given by the fact that small gallstones from a patient placed in the normal gallbladder of a cat may, after the animal is fed, produce obstruction and dilatation of the common duct, and obstruction of the cystic duct with distention of the gallbladder and acute cholecystopathy.

There is another serious danger in the presence of gallstones, "silent" or otherwise—cancer. Ninety per cent of cancers of the gallbladder are found accompanied by stones. In the other ten per cent, small gallstones, or debris, having the same causes as larger gallstones, may have been there and passed. Gallstone debris can be placed in the gallbladder of a cat, and after two weeks of normal feeding, where obstruction has not occurred, investigation will show a clear gallbladder and ducts. It is possible that the process of cholesterosis, almost surely a factor in gallstone formation, may be relieved and any resulting debris passed out by normal vesicular contractions, but leaving alterations which may become carcinomatous. Consequently, the finding of cancers in the absence of stones in ten per cent of the cases is not convincing evidence that gallstones, or their causative factors, are not associated with cancer of the gallbladder. Be that as it may, cancer will not develop in those gallbladders removed early for stones.

Instead of counseling to let the "silent" gallstone alone, how much better to avoid complications by removing the gallstone, and if possible its habitat and breeding ground, while it is still "silent". At least, let us remove it before it has gone beyond the "growling" stage. To those physicians who say: "Let the sleeping dog lie", my answer is, "Beware that he does not become a vicious, destructive beast".

The death rate of cholecystectomy in good clinics over the country is one to one and one-half per cent. But even this low percentage is what it is largely because physicians have not taken proper diagnostic measures, or have advised to let the gallstones alone. Mortality from cholecystectomy with patients carrying "silent" gallstones before complications have arisen would undoubtedly be below one-half of one per cent. The risk of complications in such cases is so great, and the risk of cholecystectomy is so slight, that I feel that a death which

occurs after operating for these complications should be laid at the door of a procrastinator.

Even though the patient is a poor surgical risk, with the improved methods of pre- and postoperative care, anesthesia, and operating technic, the risk of cholecystectomy is usually less than that of "expectant" treatment. For we can usually expect the worst. Because of the mechanical factors of anatomy and physiology, medical treatment for cholelithiasis offers nothing.

In the patient who is a bad risk, surgery still offers the best prospect; especially in the case of the "silent" gallstone. Usually in such a case the gallbladder is thin-walled and concentrates its bile normally; in other words, a normally functioning gallbladder. The stone itself is the dangerous factor. We are now finding that, contrary to our previously held notions, the stone can be removed from such a gallbladder with a normally functioning vesicle as a result. Even in the acutely obstructed gallbladder, removal of the stone may be effective. This can be done by a skillful surgeon under local anesthesia, with a small incision, little trauma to surrounding viscera, and almost no shock to the patient.

Since, then, the risk of leaving gallstones is so great, and the risk of removing them so slight, let us remove them, and thereby save lives.

MEDICAL MANAGEMENT OF BENIGN PROLAPSE OF THE GASTRIC MUCOSA INTO THE DUODENUM*

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Prolapse of the gastric mucosa into the duodenum has now become established as a definite clinical entity, rather than as a phenomenon which may exist coincidentally with other diseases of the gastrointestinal tract. This entity has been increasingly claiming the attention of investigators in recent years[1]. The incidence of the condition has not as yet been fully established. Feldman and Myers[2] have reported that in 12,321 collected cases of gastrointestinal roentgen studies compiled from the literature, the incidence of prolapse of the gastric mucosa was approximately 2.5 per cent. The roentgenologic incidence of prolapse of the gastric mucosa in patients with specific complaints of epigastric distress, however, would probably approximate 15-20 per cent. In view of this, it seems rather strange that the condition has not been more frequently roentgenologically demonstrated in recent years. This seeming paradox may have resulted from the fact that prolapse of the gastric mucosa frequently occurs coincidentally with duodenal ulcer or hypertrophic gastritis, and that the phenomenon is of a dynamic nature: "it is not uncommon to observe evidence of an extreme type of prolapse at one time and only minimal signs of prolapse during the same examination or at another time"[2].

Description

Prolapse of the gastric mucosa into the duodenum bears similarity to intestinal intussusception. The terminal section of the pyloric mucosa protrudes through the relaxed sphincter muscle of the pylorus into the first portion of the duodenum. The phenomenon becomes an illness *per se* only when the prolapsed mucosa begins to erode or to ulcerate, producing a plethora of distressing gastrointestinal symptoms. When, as a result of excess acid-pepsin activity, erosion or ulceration of the prolapsed mucosa occurs, pain, more intense than that in duodenal ulcer, is elicited. Every particle of ingested matter must necessarily travel through the pyloroduodenal passage which has become narrow as a result of partial obstruction by the prolapsed gastric mucosa. When ulceration is present, the surrounding tissues are edematous and inflamed. Thus, ingested matter, in passing, scrapes the sensitive tissue, producing the severe gastrointestinal discomfort.

Etiology

Many theories regarding the etiology of prolapsed gastric mucosa have been advanced. Among these can be listed: redundant mucosa, gastritis, in-

*The supplies of Trevidal used in this study were furnished through the courtesy of Dr. K. W. Thompson, Medical Director, Organon Inc., Orange, N. J.

creased gastric peristalsis, psychoneurotic tendencies, and chronic gastric mucosal irritation. Hypertrophic gastritis is commonly observed in association with prolapsed gastric mucosa, and therefore remains as an important etiological factor. "One must consider the effect of a mass of redundant hypertrophied gastric mucosa acting as a foreign body irritant which may be the primary stimulating cause for the initiation of the increased peristaltic activity"[2]. Markedly increased gastroduodenal peristalsis is also an important etiologic factor, since it is present in most cases of prolapse. "It should be emphasized, however, that although hyperperistalsis of the stomach must play a fundamental role in the production of this condition, it should not obscure other etiologic factors"[2]. The influence of psychic factors must also be taken into consideration. The presence of a psychoneurotic component in many patients emphasizes hypermotility of the stomach as an etiologic factor contributing to the detachment of the gastric mucosa[3].

The specific etiology of the condition is as yet unknown, although the possibility of a single factor causing the condition seems highly improbable at this time.

Symptomatology

The condition is not characterized by any definite clinical picture and frequently co-exists with other gastrointestinal affections[4]. The symptoms presented by the patient with prolapsed gastric mucosa resemble those of duodenal ulcer which is often seen in patients with prolapsed gastric mucosa. "One should suspect the presence of prolapse of the gastric mucosa in all cases that present an atypical ulcer history"[2]. No pathognomonic symptoms are presented by the patient with prolapse of the gastric mucosa. The complaint most frequently voiced by patients is that of severe epigastric distress, usually beginning one-half hour after meals (instead of the common one or two hours as in duodenal ulcer). The onset of pain can be coincided with the peristaltic movements of the stomach as it begins to empty its contents through the lesion into the duodenum. Other symptoms commonly observed in this condition are nausea and vomiting, bloating, gastric distention, belching, burning sensations, regurgitation, and diarrhea. The severe pain usually diminishes following vomiting, only to be replaced by a burning sensation which may last for days. This symptom is rather significant, for it usually indicates the presence of an obstruction. Unfortunately, physical examination usually does not reveal any significant diagnostic data. The association of duodenal ulceration with prolapse of the gastric mucosa is emphasized as being extremely common, while the incidence of gastric or prepyloric ulcer with prolapsed gastric mucosa is relatively infrequent[2]. Some degree of hypertrophic gastritis probably occurs in all cases[2].

Roentgenologic Diagnosis

Prolapse of the gastric mucosa into the duodenal bulb can only be diagnosed by careful roentgenologic examination of the stomach, based upon

pathognomonic roentgenologic criteria established for this condition[2]. The roentgenologic incidence of prolapse of the gastric mucosa into the duodenum is appreciably higher than has been estimated[2]. X-ray findings are fairly well established: the terminal section of the pylorus appears blacked out, simulating a semilunar defect. This obstruction is rarely irregular in shape. The first part of the duodenum is also included in the defect. Just beyond this, there appears an area which is typically half-moon shaped, representing the widened area of the duodenum into which an ingested barium meal flows after passing through the stricture of the prolapse*. Existing coincidentally with prolapsed gastric mucosa may be other gastrointestinal disease, such as duodenal or gastric ulcer. Feldman and Myers[2] have listed certain roentgenologic findings as being characteristic of prolapse of the gastric mucosa into the duodenal bulb, mainly: 1. defect in the base of the duodenal bulb, 2. "honeycomb," "mushroom," or lobulated defect in the bulb, 3. variations in the appearance of the bulb in the same and on repeated examinations, 4. accelerated gastric peristalsis, 5. gastric fold observed to be prolapsed into the bulb, 6. multiple linear negative defects in the pylorus representing mucosal folds passing from the stomach into the duodenum, and 7. changes in the pyloric canal; "these may be normal, narrowed, widened, or show an annular cuff of varying extent, depending upon the amount of redundant mucosal folds in the pylorus"[2]. The gastric rugae which are seen passing transpylorically into the duodenal bulb are thickened, smooth, and flexible, and the remainder of the bulb is usually completely filled out if unassociated with a true duodenal ulcer. Since the condition of prolapsed gastric mucosa is a dynamic one, subsiding and recurring with gastroduodenal peristaltic activity, the appearance of the defect may change from one roentgenogram to the next, and at times may even disappear entirely[1,5]. Gastroscopy or gastrophotography offer little aid in diagnosis, since by these methods it is difficult to distinguish prolapse from pylorospasm. Gastroscopy does aid in confirming the absence of any malignant lesion and it has helped to establish the high incidence of hypertrophic gastritis present in cases of prolapse. Additional diagnostic procedures such as fractional gastric analysis and cytologic examination of gastric washings should also be employed.

Differential Diagnosis

Clinically, symptoms of prolapse may resemble those of peptic ulcer, gastric neoplastic disease, and all types of gastritis. Roentgenologically, prolapse does not present any real difficulty in differential diagnosis, since the blacked-out area of the distal portion of the stomach and the proximal portion of the duodenum always show the regular shape of a semicircle or half-moon. Other

*In any case where there is a persistent regularly shaped filling-defect at the end of the pylorus, taking in the proximal end of the duodenal bulb, and persistent filling of the distal duodenal half, the diagnosis of prolapse has to be kept in mind.

conditions which have been reported to simulate prolapse, actually are conditions of the antrum of the stomach *per se* such as:

Hypertrophic gastritis:—In the severe case, enlarged rugae are seen involving the entire body of the stomach as compared to prolapse in which these "mushroom folds" are confined to the antrum and pyloric area and many times co-exist with prolapse.

Antral gastritis:—Lichstein[3] states that this is probably the most difficult of all conditions to differentiate from prolapse. Here the antrum appears shortened and narrowed, with evidence of pylorospasm in gastritis, and "with the presence of large gastric folds which assume a polypoid appearance"[3].

Gastric polyp:—This presents an unchangeable defect which varies in location in relation to the pyloric sphincter, whereas prolapsed mucosa is not seen proximal to the sphincter.

Prepyloric carcinoma:—The failure of peristaltic waves to pass through the antrum, and the constancy of the antral deformity are almost pathognomonic of this lesion. The sharp change from normal in contrast to the gradual transition characteristic of benign prolapse has to be noted[3].

Treatment

As with duodenal ulcer, treatment should always be medical. The place for surgery in this condition is still to be evaluated and surgery should be carried out only in the presence of complications or if intensive medical treatment fails to bring relief[3,4]. When absolutely necessary, the surgical procedure of choice is subtotal gastrectomy. The ulcerated area blocking the pyloroduodenal region should be removed and a gastrojejunostomy established. This treatment should not have to be resorted to under intelligent medical management. The only indications for surgery are:

1. Recurrent hemorrhages.
2. Pyloric obstruction.
3. Intractable pain, refractory to any form of medical therapy. This latter factor has not been encountered by the author since the use of Trevidal*.

It should be remembered that "recurrences of the phenomenon are known to take place following excision"[1].

As stated, medical therapy is the treatment of choice in this condition. Through proper medical management of the patient, it is possible for the physician to make the patient's condition inactive and completely asymptomatic. Effort should be made to enlist the complete cooperation of the patient. This may be accomplished by a thorough explanation of the nature of his illness.

*Trevidal, marketed by Organon Inc., Orange, N. J.

Antacid medication should be employed generously to reduce the excess acidity usually found in these patients. Anticholinergics or antispasmodics may be employed when necessary to reduce gastrointestinal hypermotility. Psychotherapy has an important function in relieving psychic influences on the condition. A diet of soft bland foods may be prescribed at the outset of treatment, and gradually expanded as symptomatic relief is obtained.

Most important in the medical management of prolapse of the gastric mucosa is the use of an agent which provides a protective coating over the lesion, thus making it inaccessible to further damage from acid gastric juice.

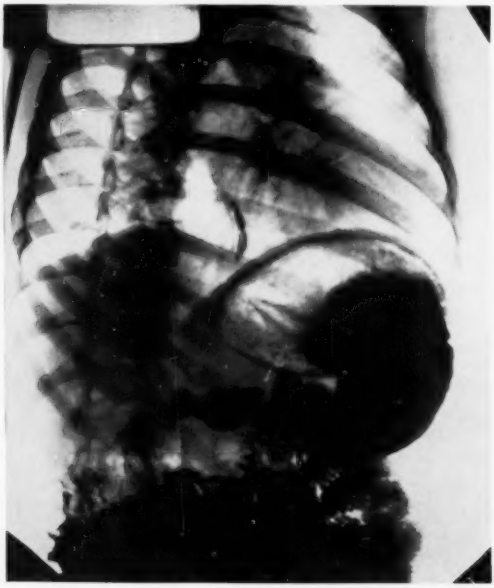


Fig. 1—(H. R. S.) Typical roentgen features of benign prolapse of the gastric mucosa into the duodenum. A 7½-year old female whose chief complaints were severe abdominal pains in the umbilical region and nausea and vomiting of 5 months duration.

Animal gastric mucins have been shown to lose their viscosity, adhesiveness, and capacity to form a protective coating even in a moderately acid medium[6] and have been shown to deposit large gummy masses unevenly in the stomach[6]. Thus they cannot be relied upon to provide any degree of protection to the prolapsed mucosa.

Because of its content of effective antacids balanced in physiologic proportions to "cancel out" undesirable side-effects while reinforcing acid neutralizing activity, along with a highly effective demulcent vegetable gum† which provides a protective colloid film on the lesion even in extremely acid gastric

juice[10], Trevidal has been employed with great success by the author in treating prolapse of the gastric mucosa. This antacid-vegetable mucin preparation has been reported on in a previous communication[7] and by others[6,8-11]. In treating patients with prolapsed gastric mucosa, Trevidal has rendered a more important service than any other antacid preparation. It provided an acid-resistant protective coating over the prolapsed gastric mucosa and neutralized gastric acid effectively, thus preventing ulceration of the prolapsed mucosa from occurring. Therefore, Trevidal must be considered the antacid of choice in treating this condition, for although it does not cure the physical prolapse, it does prevent ulceration from occurring and giving rise to the symptoms of gastrointestinal distress.



Fig. 2—(D. M.) Prolapsed gastric mucosa diagnosed by x-ray in a 33-year old white female whose chief complaints were indigestion, vomiting, and severe pains in the right epigastrium.

On a regimen of Trevidal, dietary restrictions, and psychotherapy, patients have been rendered symptom-free shortly after the institution of therapy. This has held for patients with lesions of relatively long duration as well as for others. Once symptoms have been brought under control, Trevidal therapy is continued, enabling patients to consume a full diet, including alcohol, coffee, and spices, while remaining completely asymptomatic.

No toxic effects have ever been observed from therapy with this antacid. Further, its palatability avoids a commonly observed complaint from patients.

Case Reports

Two case reports serve to illustrate the effectiveness of Trevidal in the medical management of benign prolapse of the gastric mucosa.

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†The gum of *Cyamopsis tetragonoloba* (Regonol).

Case 1:—H. R. S., a 7½-year old white female came to this office on February 14, 1955, complaining of persistent nausea, vomiting, and abdominal pains in the umbilical region for 2 weeks preceding her visit. About 5 months prior to her visit, she began to get very pale and had frequent bouts of nausea and abdominal pains. Her mother gave her baby Castoria, but this did not provide any satisfactory measure of relief. She obtained some improvement from citrate of magnesia, the pain, nausea and vomiting disappearing for about two weeks. Following this, she again experienced severe abdominal cramps, followed by nausea and vomiting. X-rays were taken on February 17, 1955, and the condition of prolapse was diagnosed. The patient was put on a regimen of Trevidal, 2 tablets 1 hour before meals, immediately following meals, and at bedtime. In 24 hours, the nausea and vomiting disappeared. After two doses of Trevidal, the abdominal cramps disappeared. The patient was also put on a Meulengracht diet. Occasionally she still gets spells of nausea, but these are usually precipitated by severe emotional upsets. After three weeks on the initial regimen, the dosage of Trevidal was reduced to 1 tablet, 1 hour prior to meals and immediately after meals, and 1 tablet at bedtime. This regimen has enabled the patient to consume a fairly full diet. She has remained asymptomatic to date, and remains on Trevidal therapy (Fig. 1).

Case 2:—D. M., a 33-year old white female came to this office in October 1954, with complaints of indigestion, heartburn, and nausea for the two months preceding her visit. In 1945, she suffered from colitis and frequent attacks of diarrhea. In 1948, emotional upset caused her to suffer a miscarriage. This was followed by a divorce. Her present complaints began at this time. Since the initial onset of her symptoms, she had been taking sedatives and antacids routinely with unsatisfactory results. The continuous vomiting and pains in the right epigastrium were diagnosed as gallbladder attacks in 1953. These attacks were most severe during periods of emotional stress and at times of menstruation. X-rays were taken late in October 1954, and revealed a condition of prolapsed gastric mucosa. On November 1, 1954, the patient was put on Trevidal, 2 tablets 1 hour prior to meals, immediately following meals, and at bedtime. Also P.R.N. After one week, the patient was completely asymptomatic. Two weeks later, the dose was reduced to one tablet before meals and immediately after meals, and P.R.N. The patient has remained symptom-free, even after the dose of Trevidal was reduced further to 1 tablet prior to retiring and P.R.N. Through use of Trevidal, the patient has been put on a reducing diet of 500 calories per day, without any deleterious effects on the prolapsed mucosa (Fig. 2).

Summary

1. Benign prolapse of the gastric mucosa into the duodenum may be defined as a condition in which the terminal section of the pyloric mucosa protrudes through the relaxed sphincter muscle of the pylorus into the first portion of the duodenum.

2. Benign prolapse of the gastric mucosa can be demonstrated roentgenologically in a greater number of patients with gastrointestinal disorders than has heretofore been recognized.

3. The phenomenon may occur with or without co-existing duodenal or gastric ulcer and all types of gastritis, although these conditions frequently accompany prolapse.

4. The specific etiology of the condition remains unknown. Redundant mucosa, gastritis, increased gastric peristalsis, psychoneurotic tendencies, and chronic gastric mucosal irritation are all of etiologic significance.

5. As with duodenal ulcer, treatment should be medical whenever possible.

6. Outstanding success in the medical management of the condition has been achieved through use of Trevidal.

7. Trevidal does not cure the physical prolapse, but it does prevent it from ulcerating and giving rise to symptoms of gastrointestinal distress.

8. This antacid preparation must be considered the medical treatment of choice for prolapsed gastric mucosa because of its remarkable ability to provide a protective, viscous coating over the prolapsed mucosa, even in extremely acid gastric juice, thus preventing ulceration from occurring.

9. Case reports illustrating the effectiveness of Trevidal in this condition are presented.

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A CLINICAL EVALUATION OF A NEW BUFFERED ANALGESIC AGENT

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Continued basic research and clinical studies concerning aspirin are justified by its leading position as a therapeutic agent, as well as by reports of irritancy of the gastric mucosa when administered alone[1,2]. Endeavors to produce nonnarcotic analgesics which are superior to aspirin have taken several courses. One has been the synthesis and evaluation of new compounds. Up to the present time, this has yielded no satisfactory substitute for aspirin. Another

TABLE I

DEGREE OF RELIEF FROM BUFFERED A.P.C. WITH TIME OF ONSET

(Onset Time—minutes)

Relief	None	0-10	10-20	20-30	30-60	Total	Per Cent
None	18					18	1.1
Slight		11	30	40	11	92	5.4
Moderate		6	19	24	3	52	3.1
Complete		10	1483	36	2	1531	90.4
Total	18	27	1532	100	16	1693	100.0
Per Cent	1.1	1.6	90.5	5.9	0.9	100	

approach has been that of enhancing the action of aspirin through the use of synergists, such as phenacetin and caffeine. This combination, popularly termed "A.P.C., P.A.C.", etc., has enjoyed extensive use. A third method of improving aspirin has been aimed at reducing the gastrointestinal symptoms associated at

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times with its ingestion. Enteric coating of tablets has been advocated but creates stability problems. Soluble salts of aspirin are recommended by some writers[2] but have not proven acceptable in practice. Concomitant administration of alkaline substances, such as sodium bicarbonate, was found to be advantageous in earlier decades. More effective acid buffering power without acid rebound may be provided by basic aluminum, magnesium, and calcium compounds, two of these being combined with aspirin in a product at present in use.

Since increased potency is ascribed to the synergistic action in A.P.C. combinations, and better tolerance and faster absorption is attributed to the alkaline substances used with aspirin, it appeared promising to combine both modes of improving the analgesic agent in one formulation. Such a tablet, a buffered A.P.C., might offer all these advantages in one preparation. Its production was not easy because of pharmaceutical difficulties overcome only recently. This specially-formulated tablet (which is referred to in this study as Medication #1), contains aspirin, 3 gr., phenacetin, 2 gr., caffeine, ¼ gr., and sufficient aluminum and magnesium hydroxides to neutralize up to 37 c.c. of N/10 HCl*.

TABLE II

INCIDENCE OF SIDE REACTIONS TO BUFFERED A.P.C. AND BUFFERED ASPIRIN
(Two Tablets per Dose)

	Medication #1		Medication #2	
No. of Doses Given	1693		521	
Type of reaction	Number of Complaints	Per Cent	Number of Complaints	Per Cent
Epigastric pain or burning	7	0.4	8	1.5
Uneasy or gaseous feelings or eructation	30	1.8	19	3.6
Nausea without vomiting	5	0.3	0	0
Vomiting	2	0.1	1	0.2
Dizziness	0	0	2	0.4
Total percentage incidence		2.60		5.76

*Provided as "Falgos" by The Sterling Winthrop Research Institute, Rensselaer, N. Y.

With the availability of this type of analgesic, it becomes desirable to determine the clinical profile of the product. In this paper is reported a statistical study of the incidence and degree of relief, speed of action, and the incidence of side-effects accompanying the use of this new analgesic agent in the treatment of various aches and pains. A parallel study has been made with a buffered plain aspirin tablet (Medication #2)† in order to compare the two products with regard to total incidence of relief from pain and of side-effects. Thus, this study provides data from which may be determined whether the addition of alkaline materials to an A.P.C. preparation results in an effective and well-tolerated product, and whether the buffered A.P.C. tablet has advantages over plain alkalinized aspirin.

The subjects employed in this study were patients in a 1,200 bed chronic disease hospital.‡ The two test medications were routinely substituted for the analgesic agents commonly employed in this institution. A total of 713 patients received 1,693 administrations of Medication #1, and 433 patients received 521 doses of Medication #2. Each dose consisted of two tablets of the test medication. Figure 1 shows the front and reverse sides of the form used by the nurses for recording the observations.

The complaints treated were those for which mild analgesics are usually considered appropriate, such as various musculoskeletal aches and pains, and headaches. The range of the ages of the patients was 27 to 86.

Table I summarizes the results obtained in the patients who received the buffered A.P.C. (Medication #1). Some degree of relief was provided in 98.9 per cent of the 1,693 administrations. This relief was reported to be complete in 90.4 per cent of the trials. Relief occurred within less than 20 minutes in 92.1 per cent, and within one hour in all cases when obtained.

Table II lists the types of complaints that were associated with this medication. The total incidence was 2.60 per cent, approximately two-thirds of which consisted of gaseous or uneasy feelings in the abdominal area. Epigastric burning, pain, nausea or vomiting occurred in only 0.7 per cent of administrations. Of considerable interest is the fact that only one side-effect is known to have occurred after the 1,531 doses which provided complete relief of pain. Thus, practically all side-effects occurred when the original complaints were only slightly to moderately relieved, if at all. This suggests that there may be a relationship between disappointment with the therapeutic effects and the reporting of symptoms listed in the table.

Of 521 administrations of buffered aspirin, relief of some degree occurred after 490, or 94.1 per cent.

†Buffered Aspirin.

‡Long Island Hospital, Boston, Mass.

Directions on reverse side

OBSERVATION FORM (Use large card)

Medication Institution.....

	Name	Sex M or F	Age	Wt.	Disease or Symptom	Severity 1	2	3	Adm. Time	Onset of Relief Min. 0-10	10-20	20-30	30-60		Degree of Relief None	Slight	Mod.	Compl.	Side-effects O	B	P	N	G	U	Observer's Initials
1																									
2																									
3																									
Etc.																									
Etc.																									
	Totals																								

OBSERVATION FORM

DIRECTIONS:

Put name of institution on each card.
The dose is 2 tablets which may be repeated every 4 hours. Chart each observation.
Do not give medication within ½ hour before meals and 1 hour after.
Follow protocol carefully—omit nothing.

Under side-effects:

O—None
B—Burning sensation in chest or stomach
P—Pain
N—Nausea. If vomiting, write in
G—Gas or burping
U—"Uneasy" sensation in stomach

Sign (initial) every observation

Fig. 1

The side-effects attending the use of buffered aspirin (Medication #2) are recorded in Table II, where they may be compared with those of Medication #1. The total incidence of untoward reactions was 5.76 per cent in Medication #2, and 2.60 in Medication #1. Side-effects were therefore of a low order in both medications, but were less frequent in Medication #1.

Comparison of Results—Medication #1 vs. Medication #2

Table III summarizes comparable values among results described above. The total incidence of relief, mild to complete, with Medication #1 was 98.9 per cent. When compared with the 94.1 per cent for Medication #2, the difference is calculated to be statistically significant by use of the Chi square test.

TABLE III

Comparison of Buffered A.P.C. (Medication #1) and Buffered Aspirin (Medication #2)

	Medication #1	Medication #2
Incidence of relief from aches and pain	98.9%	94.1%
Statistical reliability of difference	t=4.57	p=0.001
Incidence of side-effects	2.60%	5.76%
Statistical reliability of difference	t=2.84	p=0.005

Likewise, the twofold greater incidence of side-effects from Medication #2 than from Medication #1 is found to be valid by this test.

Further analysis did not reveal significant correlations between the incidence or degrees of relief on the one hand, and age, weight, disease or symptom, its severity, or the time of administration on the other. The occurrence of side-effects in the two series was likewise unrelated to these factors.

Summary

1. A new analgesic tablet, Buffered A.P.C., in which the buffering agents, aluminum and magnesium hydroxides, have for the first time been successfully combined with aspirin, phenacetin, and caffeine, was administered 1,693 times to 713 chronically ill hospitalized patients for the relief of various types of

aches and pain. The dose used was two tablets. The total incidence of relief was 98.9 per cent, and complete relief was obtained in 90.4 per cent of the tests.

2. The administration of a plain buffered aspirin, in the same dose, 521 times to 433 patients, resulted in a total incidence of relief of 94.1 per cent. The difference in clinical effectiveness was found to be statistically significant.

3. Relief occurred within 20 minutes after 92.1 per cent of the Buffered A.P.C. administrations, and within one hour in the remaining cases where it was effective.

4. Side-effects were reported in 2.6 per cent of cases with Buffered A.P.C., as compared to 5.8 per cent with Buffered Aspirin. This difference also was calculated to be statistically reliable.

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TREATMENT OF PEPTIC ULCER BY USE OF INTRAMUSCULAR TRYPSIN

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Peptic ulcer continues to be one of the baffling problems of medicine. Despite new and apparently improved methods of treatment developing each year, nothing of real significance has been added recently. The developments are for the most part variations on the theme of acid neutralization and reduction of motility and of secretion.

The etiology of peptic ulcer is obscure because of the variety of factors known to influence ulcer production. It is generally accepted that it represents a form of local destruction of tissue which occurs because of the eroding action of acid chyme. A local disturbance in the processes of resistance renders the tissues unable to protect themselves from dissolution. For the ulcer to form there first must be an erosion of the mucus layer, followed by a breakdown of the second layer of defense. This second protective layer consists of surface cell desquamation with emptying of thecal cavities to release very viscous mucus. If the rate of regeneration of the cells lags behind the rate of desquamation, denuding of the mucosa will progress until the layer of gastric glands is exposed or even destroyed and acute peptic ulcer results[1].

Hollander further points out that ulcer formation is dependent more on susceptibility to autodigestion of the gastrointestinal mucosa than to excessive secretion of gastric juice, since peptic ulcers can occur in persons with normal or low acid production. And when an ulcer does occur, it is usually limited to a single site in a circumscribed area rather than diffusely throughout the surface of the total area subjected to the same surface conditions.

In the treatment of peptic ulcers, the time-tested methods of modifying the gastric environment by acid neutralization and inhibition of secretory mechanisms are successful in most cases. It would, however, seem rational to attempt to treat the systemic environment of the ulcerated area as well.

Assuming that an ulcer occurs at a fault in the protective barrier, the localized defect may be due to the inability of the surface cell to secrete mucus, or it may be due to a reduced rate of regeneration of cells. A major cause for either condition could be a lowered blood supply to the affected area. In fact, the probable mechanism for the well-recognized psychosomatic component in ulcer formation is an interruption of blood flow in a localized area. Wolf and Wolff's[2] experiments have shown a striking alteration in blood supply to the mucosal surface in a subject under emotional stress. There is some evidence that gastric ulcer is due to a generalized circulatory insufficiency which is intensified in focal areas of the stomach[3]. Circulatory dysfunction has been

implicated repeatedly in the formation of peptic ulcers, probably through interference with local nutrition. Swelling and inflammation of the ulcer border and around the crater may be added factors in maintaining circulatory stasis.

Intramuscular trypsin has been reported to increase local blood supply in inflamed areas[4], to increase local drainage and restore fluid balances in venous and lymphatic stasis[5], and in general to reverse inflammatory processes[6]. The mechanism has been attributed to the ability of the enzyme to remove soft fibrin or inflammatory barriers and plugs. In the more chronic states, the action of trypsin is slower and more difficult to evaluate, but here too there is evidence of improved local metabolism. These properties should be equally applicable to the treatment of peptic ulcer. If the enzyme could promote healing by providing a better medium for repair and regeneration, the peptic ulcer patient given trypsin should recover more rapidly and possibly more completely than the patient treated without trypsin.

To assess this hypothesis, a group of ten patients was selected and treated with trypsin. None of the patients had responded to previous treatment because they would not or could not submit to a strict dietary regimen and to enforced rest, nor could their psychogenic or neurogenic environments be altered sufficiently to make any difference in their life situation. Trypsin was added to their treatment with no other change in the regimen. Injections of 2.5 mg. of trypsin (as 0.5 ml. of Parenzyme•) were given deep in the buttocks once daily for seven days, then every other day for the second week and once weekly thereafter.

Eight of the ten patients responded dramatically within one week with complete subsidence of subjective symptoms such as pain and heartburn. One patient whose ulcer had perforated and was walled off by the pancreas was started on trypsin, but after two days was considered too great a risk for further medical management. A subtotal gastrectomy was performed with an uneventful recovery. The tenth case was complicated by tabetic crisis and did not show improvement with trypsin until antiluetic treatment had been instituted.

The use of alkalis and antispasmodics was diminished or completely eliminated and a balanced diet was well tolerated by the end of the third week in every one of the eight cases. It has not been possible to evaluate the healing process with radiologic studies at this early level.

Case Reports

Case 1:—Mr. S., age 40. Pain in the epigastric region with confirmed ulcer of the duodenum of two years duration. Had been taking Amphojel and belladonna in conjunction with a modified Sippy diet. Temporary relief only on

•Parenzyme: The National Drug Company, Philadelphia, Pa.

this regime. With Parenzyme, 0.5 c.c. deep intragluteally daily for seven days, there was complete subsidence of symptoms. Injections were continued every other day the second week and once weekly thereafter.

Case 2:—Mr. B., age 43. Ulcer preduodenal (prepyloric) by x-ray, duration four years. No apparent relief of symptoms because he could not conform to Sippy diet regime. Treatment with Parenzyme following the same course of intramuscular injections as in the preceding case gave relief by the second day. A full diet was tolerated without any discomfort.

Case 3:—Mr. T., age 28. Peptic ulcer for 6 months with relief periods of inadequate control. The injections will be withdrawn as the patients appear to be in adequate condition to resist ulcer breakdown.

Comment

This report is presented as a preliminary observation with the hope that others will use trypsin (Parenzyme) for its effect in restoring local circulation in their peptic ulcer patients, and will appraise the results critically. That eight of ten patients who had not responded to admittedly inadequate diet-antacid-antispasmodic therapy did respond when intramuscular trypsin was added to the therapeutic program, appears to have some significance. No side-effects or toxic symptoms were observed. All injections were made with a clean dry needle and were given deep in the muscle.

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INTRAVENOUS AND ORAL CHLORAMPHENICOL (CHLOROMYCETIN) IN THE POSTOPERATIVE TREATMENT OF ENTERIC PERFORATION COMPLICATING TYPHOID FEVER

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Previously the author[1] has reported a 3.5 per cent incidence of intestinal perforation in a series of patients with typhoid fever. This is a report on 26 patients treated for intestinal perforation. In 2 of these patients perforation occurred while under treatment for typhoid fever in K.E.M. Hospital, Bombay. The remaining 24 patients were admitted directly to K.E.M. surgical service with a diagnosis of perforation, or transferred from the City Fever Hospital because perforation was suspected.

There were 23 male and 3 female patients in this series, 8 patients were 11 to 20 years old, 4 were 21 to 30, and 14 were 31 to 40.

Clinical Picture

Sudden pain during the course of fever marked the onset of perforation in all 26 patients. Pain usually started in the umbilical region and was acute and colicky. In one patient the pain started after an enema which the patient had administered to himself to relieve constipation.

Table I lists the signs and symptoms observed and their frequency of occurrence.

TABLE I

Frequency of Pains and Symptoms

Signs and Symptoms	Patients
Pain	26
Vomiting	7
Diarrhea	5
Constipation	4
Distention	21
Tenderness	26
Rigidity	26
Shifting dullness	12
Obliteration of liver dullness	24

*Honorary Assistant Surgeon, K.E.M. Hospital, Bombay.

Preoperative Diagnosis

Free gas was seen under the diaphragm on x-ray in all the 26 patients. Intestinal perforation was diagnosed preoperatively in all patients and subsequently confirmed at operation.

TABLE II

Survival Rate as Related to Interval Between Onset of Pain and Operation

	Cured	Expired	Total
Operated within 12 hours	8	—	8
Operated within 24 hours	9	—	9
Operated after 48 hours	5	1	6
Operated after 3 days or more	1	2	3
Total	23	3	26

Survival rate, as may be seen in Table II, was directly related to the duration of the intestinal perforation. Mortality was high among those patients with generalized peritonitis.

Investigations

Routine examinations of urine, blood pressure, blood culture, blood cytology, triple Widal, x-ray of abdomen, and culture of peritoneal exudate were carried out. The Widal reaction was repeated during chloramphenicol therapy and at the time of discharge. The triple Widal reaction was positive for *Salmonella typhosa* in a dilution of 1:250 or 1:125 in 23 cases and it was positive for S. *paratyphi* A in 3 cases.

Site and Incidence of Perforation

In all 26 patients the perforation was found in the last two feet of the ileum and in each one only a single perforation was detected. In one patient two degenerated Peyer's patches appeared to threaten additional perforation and purse-string sutures were placed around them as a safeguard.

Anesthesia and Anesthetic Agent

In the first patient an endotracheal cyclopropane anesthesia was used. In three operations endotracheal ether was used. Subsequently it became a routine to perform operations on all patients under spinal anesthesia using 1.2 to 1.4 c.c. Nupercaine. Saline, blood, and ephedrine were given to combat any fall in blood pressure.

Operative Procedure

A uniform procedure was used in all patients. A midline suprapubic, infraumbilical incision was used to expose the terminal ileum. When the perforation was located, it was closed with a purse-string suture.

In the first patient intestinal catgut was used, but leakage occurred on the ninth postoperative day. The patient was operated upon four times and died on the 23rd day after the first operation. In retrospect it was thought that catgut produced a digestive reaction in the bowel wall resulting in marked edema and softening which greatly favored leakage through the closed perforation. Linen was used in all subsequent operations and reoperation was not required. A small piece of omentum or a piece of peritoneum from the wound edge was sutured over the closed perforation.

Peritoneal exudate was aspirated and collected for culture. Swelling of Peyer's patches and acute mesenteric lymphadenitis were observed in all patients. A No. 12 or No. 14 catheter was left in at the lower end of the incision and the abdomen was closed in layers.

After the wound was closed, a solution containing 1 gm. of dihydrostreptomycin and 1,000,000 units of penicillin sodium in distilled water was injected through the catheter into the peritoneal cavity.

Postoperative Treatment

The retained catheter served as a drainage tube, and was also used for daily intraperitoneal instillation of streptomycin and penicillin after the operation. The usual daily dosage was 1 gm. of dihydrostreptomycin and 500,000 units of penicillin sodium in 10 c.c. of distilled water. The catheter was removed after the fourth postoperative day as soon as the patient's temperature and general condition showed sufficient improvement.

Routine postoperative treatment, in addition to the local therapy described above and the use of chloramphenicol, consisted of parenteral penicillin and streptomycin; blood transfusion, 500 c.c. to 1,000 c.c.; and glucose saline 2,000 c.c. or more daily.

Chloramphenicol Therapy

Only 2 patients received oral chloramphenicol before they were admitted to surgery with a diagnosis of perforation.

Chloramphenicol is only slightly soluble in aqueous media and so is not convenient to be used intravenously as such. When dissolved in propylene glycol, a 15 per cent solution can be obtained but precipitates when it comes in contact with water or saline. Further, propylene glycol like other alcohols is an irritant and tends to produce venous thrombosis.

Chloramphenicol dissolved in a solution of acetyl dimethylamine does not precipitate when diluted by saline or water. The 2 c.c. ampoules used in this investigation contained 0.5 gm. of chloramphenicol in a 25 per cent solution.

As the first dose, 1 to 1.5 gm. chloramphenicol diluted with glucose saline was given at the time of operation. Subsequently, 0.5 gm. with saline was given intravenously two or three times a day depending on the fever, toxemia, and general condition of the patient.

The total dose used intravenously varied between 4 gm. and 13 gm. in the patients that survived, while in 2 out of the 3 that died only 1.5 gm. and 2 gm., respectively, could be given.

Results show that intravenous chloramphenicol has distinct advantages over oral therapy; absorption is certain, and continuous aspiration of the bowel contents can be satisfactorily maintained. None of the patients experienced serious complications. Thrombosis of the veins was observed in only 2 patients and here the venous cannula may have been responsible.

When their general condition improved, the patients were given chloramphenicol. Dosage was 4 capsules (1.0 gm.) initially, followed by 2 capsules (0.5 gm.) three or four times a day, then gradually reduced and finally discontinued. The average total oral dose given was 15 gm. to 25 gm.

Comment

Prior to the use of chloramphenicol, treatment of intestinal perforation was unsatisfactory. Romanis and Mitchiner[2] stated that "the mortality of typhoid perforation treated by operation is at least 70 per cent". Dunkerly[3] reported a mortality of 55.5 per cent in a series of 22 patients while Lozoya[4] showed 12 deaths in 21 patients. These low figures without chloramphenicol therapy can only be explained as the result of including patients with paratyphoid fever or mild forms of enteric fever. Baliga[5] reported 17 survivals out of 128 operations at K.E.M. Hospital between 1940 and 1948, a mortality of 86.8 per cent. Mehta[1] reported a mortality of 43.3 per cent in an analysis of 30 patients that received oral chloramphenicol therapy.

In this series of 26 patients treated with intravenous and oral chloramphenicol, there have been only three deaths, 11.53 per cent.

Summary

In 26 patients with typhoid fever, intestinal perforation was treated with oral and intravenous chloramphenicol and intraperitoneal and parenteral penicillin and streptomycin. There were only three deaths in this series. One of the 3 patients died on the 23rd postoperative day possibly due to the use of

a catgut suture rather than linen. The other 2 died within 48 hours of operation before adequate intravenous chloramphenicol could be administered.

Recently, chloramphenicol for intramuscular administration has been made available and it has been used successfully in one patient not included in this series.

Chloromycetin, the brand of chloramphenicol used for this study was supplied by the courtesy of Messrs. Parke, Davis and Company, Limited.

Thanks are due to the Dean, K.E.M. Hospital, and to the Honorary Surgeons for all facilities made available and cooperation given.

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HISTOPATHOLOGIC ASSOCIATION BETWEEN REGIONAL ILEITIS AND GIANT FOLLICULAR HYPERPLASIA

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Since 1932 when Crohn and his associates classified regional ileitis, this clinicopathologic entity has been reported more frequently in succeeding years. As the disease progresses from the stage of acute inflammation to suppuration and through the complicating phases of abscess and fistula formation; it progressively changes from a medical to a surgical problem. Therefore this disease is of great concern from the aspect of surgical pathology.

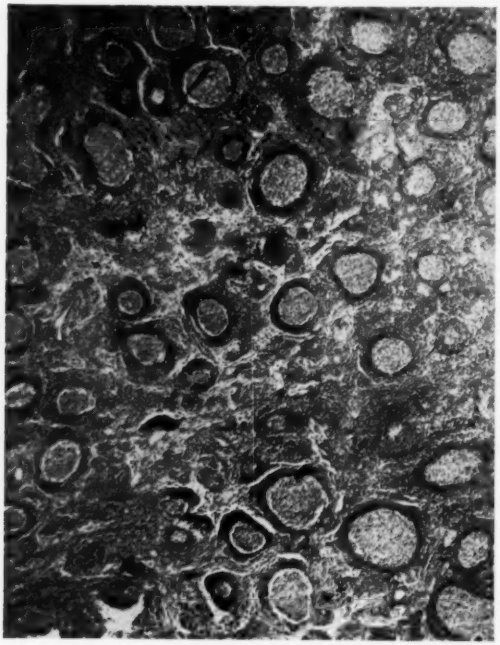


Fig. 1—Very low power photomicrograph, showing numerical and dimensional hyperplasia of the lymph follicles in giant follicular lymphadenopathy, with an extensive degree of interfollicular fibrosis. (Symmers: Arch. Path., Sept., 1938.)

Thus any presentation which attempts to elucidate the underlying pathology of ileitis is of interest to the surgeon as well as the internist and the pathologist. It is the purpose of this essay to advance a histopathologic association

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between regional ileitis and follicular hyperplasia as seen in certain pathologic conditions found in lymph nodes and the spleen. In order to do this systematically a brief discussion on giant follicular hyperplasia will be presented and the comparative similarity to the changes seen in ileitis will be unfolded.

In 1938 when Symmers emphasized giant follicular lymphadenopathy, it was rightly termed "a comparatively newly recognized form of disease involving the lymph nodes". His interest in this disease entity resulted in several

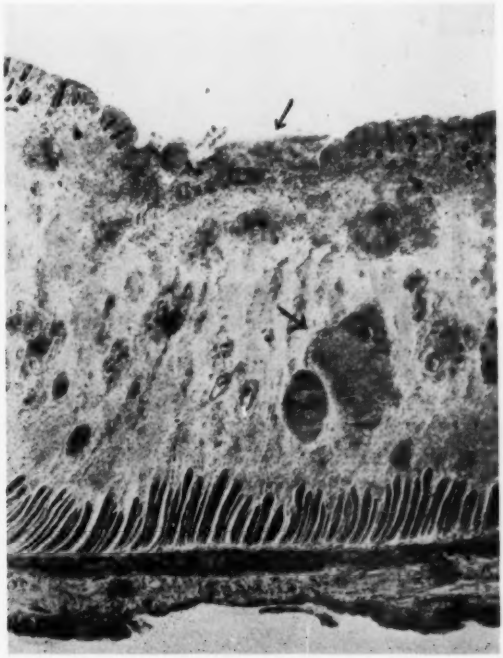


Fig. 2—Photomicrograph of ileum (x-10) showing early lesion of ileitis. Upper arrow indicates ulceration in mucosa. Other arrow marks lymphoid hyperplasia. The submucosa is distended due to obstructive lymphedema. (Hadfield: The Lancet, 7 Oct., 1939.)

publications which, in a great measure, portrayed the true pathologic nature of this form of lymphadenopathy. It is from these publications that the following discussion has been abstracted[1,3].

Histologically, giant follicular lymphadenopathy is dissimilar to other specific lesions as Hodgkins' disease, lymphosarcoma and lymphatic leukemia which are associated with enlargement of lymph nodes. In giant follicular

hyperplasia the nodes show replacement of their normal architecture by dimensional and numerical hyperplasia of the follicles (Fig. 1).

Two types or groups have been described by Symmers. In the first group the hyperplastic follicles in the lymph nodes maintain their structural identity for months or years, or the nodes may undergo reduction in size or disappear temporarily for no apparent reason, or they may show histologic signs of healing irrespective of treatment, or they may rupture spontaneously. (This seems

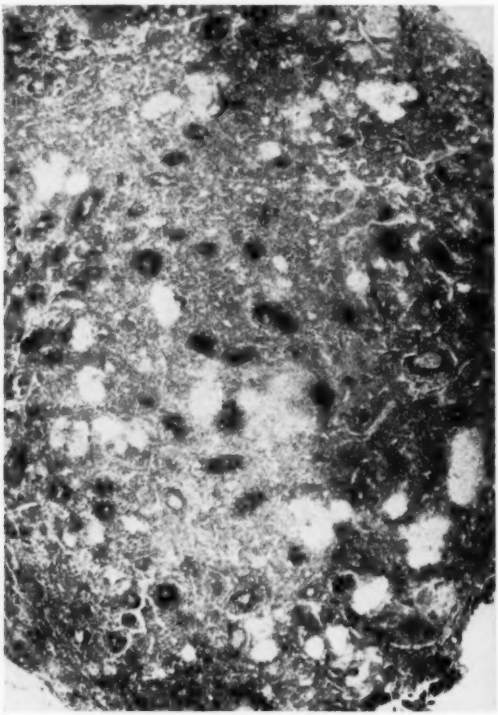


Fig. 3—Section of lymph node removed from specimen of ileum with segmental ileitis. This lymph node reveals conspicuous pale areas of giant-cell formation which are similar in type to the cells seen in Fig. 1 showing giant follicular hyperplasia (Hadfield: The Lancet, 7 Oct., 1939.)

to fall into the same pathways which may be taken by the pathologic processes of regional ileitis.)

The second group of follicular hyperplasia alters its course and patterns itself as a unique disease characterized by late necrotic lesions in the follicles of lymph nodes which leads one to suspect a mutation form of giant follicular hyperplasia[1].

Regional ileitis simulates the first group in which cytologically the follicles are distinguishable only with difficulty from those found in lymph nodes showing the familiar hyperplasia which occurs in association with innumerable inflammatory lesions. A complete understanding of the fundamental changes in follicular hyperplasia is lacking. Knowledge of the disease has been obtained from the study of excised lymph nodes and a few spleens removed at operation. The term "giant" is used because the lymph follicles appear "giant size" under the microscope. It is primarily an inflammatory lesion with the seat of the disease found in hyperplasia of the lymph follicle[3].

Hadfield, in England, was the first author to publish his observations which suggested that the pathologic site of regional ileitis was to be found in the lymphatic system of the gastrointestinal tract[2]. Thus it is understandable why regional ileitis occurs more frequently in those segments of the small intestine, i.e. ileum, wherein more lymphatic channels are present. This lymphatic site of origin is in keeping with the gross pathologic findings at the time of surgery. When a resected specimen is opened the following three pathologic changes are noteworthy[4]: 1. Marked thickening of the bowel wall. 2. Narrowing of the intestinal lumen. 3. Varying degrees of mucosal ulceration, destruction and hyperplasia.

Gross inspection suggests that the "thickening" involves all layers of the small intestine. Closer visualization, however, reveals that the greatest increase in width of the intestinal segment is in the submucosa[3]. It is this layer that contains the lymphatic structures. The intramural lymphatic system is more developed in the ileocecal region of the small intestine and quantitatively diminishes proximally up to the ligament of Treitz and the duodenum. This is also in keeping with the knowledge that the maximum involvement in the classic instance of regional ileitis is in the extreme terminal portion of the ileum just proximal to its junction with the cecum. (Hence the origin of the descriptive term "terminal ileitis".) It is assumed that the lesion commences in the terminal ileum and gradually extends proximally in the ileum[4].

The histologic studies on regional ileitis by Hadfield demonstrated that the submucosal swelling was due to: 1. Hyperplasia of lymphatic tissue. 2. Obstructive lymphedema.

These findings definitely indict the lymphoid tissue as the site of origin in this disease. The characteristic findings being lymphoid hyperplasia with giant-cell systems in the submucosa and in the lymph nodes[2,4].

As previously mentioned ileitis has an affinity for lymphatic structures in the intestine. These same structures are more frequently involved in mesenteric lymphadenitis and in intestinal tuberculosis. Thus the origin of the thought, in years past, that regional ileitis was associated with or was a form of tuberculosis is understandable.

The complications of ulceration and subsequent abscess and/or fistula formation may possibly be explained on the basis of lymphatic blockage. This type of blockage causes localized edema. Edema by direct pressure and stagnation results in stagnant, and ischemic tissue anoxia. Anoxia of long duration inevitably expresses itself in tissue necrosis. Localized tissue necrosis is the point of origin for ulceration and its concatenation of complications.

A further confirmation for the importance of lymphatic obstruction in the pathogenesis of regional ileitis has been found experimentally by Reichert and Mathes[6]. These investigators produced chronic edema of the ileum by injecting irritants and sclerosing solutions into the mesenteric and submucosal lymphatics of experimental animals. Examination revealed thickening and edema of the small bowel wall, especially the submucosa and muscularis, associated with pathologic changes similar to those seen in the regional ileitis which occurs in human beings.[4,6].

A comparison of the microscopic section taken from a proven case of giant follicular hyperplasia and that taken from a proven case of regional ileitis (see illustrations) reveals the similarity between these two clinicopathologic entities. Of a certainty the large follicles are more numerous in the section of lymph node since it is a lymphomatous structure. The lymphatics are less numerous in the small intestine by comparison because of dissimilar physiologic function. In this latter situation the intestinal lymphoid tissue is intimately associated with the process of absorption by the mucosa. This would suggest that the lymphoid cells are present for the purpose of filtration rather than as vascular lymphatic channels in which lymph nodes play a prominent part.

The close relationship between the lymphoid tissue and the mucosa further substantiates the *modus operandi* of the development of mucosal ulcerations resulting from lymphedema as previously described in the pathologic physiology of regional ileitis.

The conclusive evidence for the lymphomatous concept of regional ileitis is to be found in the study of adjacent mesenteric lymph nodes which demonstrate the conspicuous pale areas of giant-cell system formation.

The evidence advanced in this discussion is presented in order to call attention to the similarity between the underlying pathology of regional ileitis and giant follicular lymphadenopathy. The pathologic picture of regional ileitis as revealed under the microscope lends credence to the supposition that this lesion is an intestinal mutation form of follicular hyperplasia.

Conclusion

Succinctly, it may be postulated that the disease variously known as chronic cicatrizing ileitis or enteritis, terminal or distal ileitis, chronic interstitial enteritis, chronic segmental ileitis or enteritis, and regional ileitis is a specific disease

of exact unknown cause producing a pseudocharacteristic lesion similar to giant follicular hyperplasia a unique disease of lymph nodes. The histopathology of regional ileitis is readily distinguishable from other specific granulomatous lesions as tuberculosis and sarcoidosis.

In view of the similarity between the histopathologic architecture of regional ileitis and follicular hyperplasia, it is proposed that regional ileitis is an intestinal variant of follicular hyperplasia. It may therefore be interpreted as a lymphomatous lesion of the small intestine to be classified under benign giant follicular hyperplasia with lymphadenopathy.

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REMOVAL OF LARGE SESSILE POLYPS OF THE RECTUM

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Large sessile polyps of the rectum require surgical removal by means other than the use of the electric cautery since these tumors, which are malignant or potentially so, may invade the wall of the rectum to such a degree that safety demands removal of the full thickness of the wall. In addition, lesions on the posterior wall of the ampulla of the rectum offer slightly more difficulty in removal by fulguration because of position. The removal of large sessile polyps of the rectum by external operation is simple.

Fulguration of large sessile polyps of the rectum is not a safe operation. Since the extent of invasion of the wall of the rectum is not known, the depth to which fulguration must be carried to remove or kill all malignant cells will also not be known.

David[2] recommended removal of such polyps by cutting the rectum up to the level of the coccyx. The tumor was pulled downward and removed by the cutting cautery going through the submucosa. Bleeding points were ligated. A continuous suture of catgut approximated the mucosa on both sides of the defect. The wall of the bowel was closed with sutures of fine catgut in the submucosa. The muscle was sutured with interrupted sutures of catgut. A row of sutures was placed through the areolar tissue over the bowel and included the extensions of the external sphincter muscle to the coccyx. The external sphincter muscle was united separately by two interrupted sutures of catgut. Some leakage along the suture line occurred about the sixth day but in all of the patients healing was effected without a fistula having been present. A carcinoma did not develop in any of the patients. One patient had a small local recurrence of the papilloma which was cured by fulguration with the patient having been well for over five years.

Blaisdell[1] advocated the anal delivery of polypoid and sessile tumors of the rectum. A sponge forceps was inserted through a resectoscope and the tumor was grasped. The resectoscope and the sponge forceps were withdrawn together until the tumor was delivered. The mucosa around the tumor was grasped with Allis forceps and the tumor was removed. A limited removal of the full thickness of the rectal wall around the tumor was permitted by this method but the amount of normal wall removed was conditioned by the height of the tumor in the rectum and the ease of delivery. It is not a safe operation for sessile polyps which must be suspected of being malignant.

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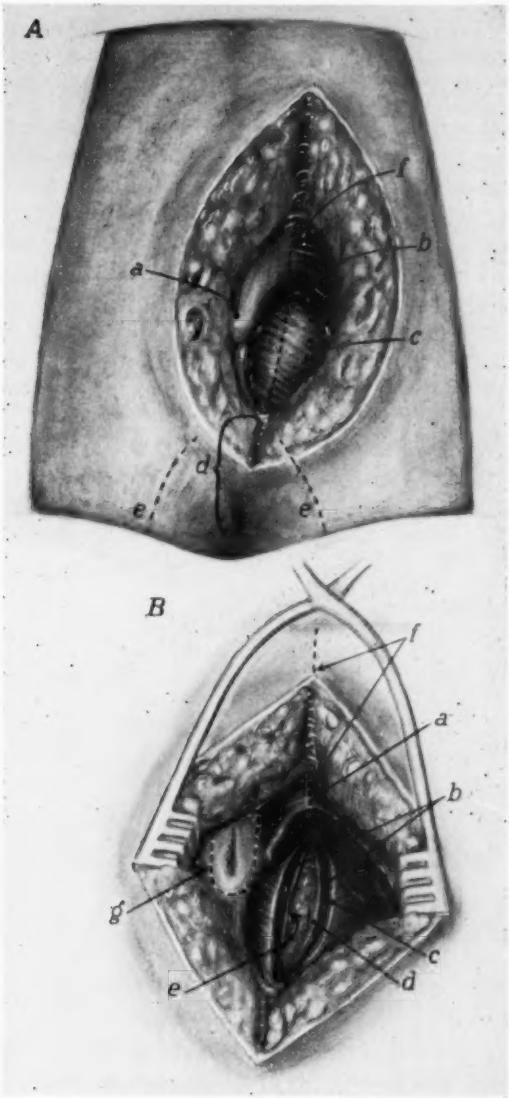


Fig. 1—Removal of sessile polyp of rectum

A. Incision:—*a*. Coccyx, *b*. Gluteus maximus muscle, *c*. Levator ani muscle, *d*. Distance of end of incision from anus which is about 3 cm., *e*. Outline of sphincter ani externus muscle, *f*. Incision in gluteus maximus muscle.

B. Deeper dissection:—*a*. Incision in gluteus maximus muscle, *b*. Levator ani muscle, *c*. Inferior layer of diaphragmatic part of pelvic fascia, *d*. Superior layer of diaphragmatic part of pelvic fascia, *e*. Retrorectal space, *f*. Additional incision to provide exposure for removal of coccyx if this is necessary, *g*. Incision for removal of coccyx if this is necessary.

Large sessile polyps of the rectum can be removed safely by excision of the full thickness of the rectal wall around the tumor. This can be accomplished without operative division of the anal sphincters, a procedure which of itself may produce an incontinent muscle and its attendant difficulties.

Sulfasuxidine and aureomycin given by mouth or sulfasuxidine by mouth and penicillin and streptomycin systemically in various combinations were used

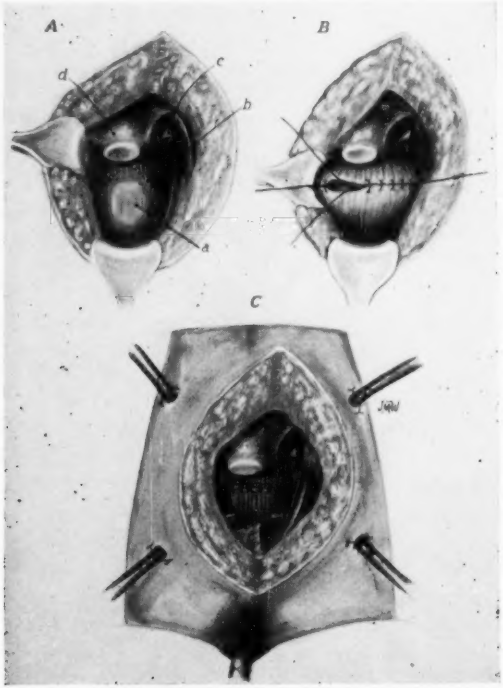


Fig. 2—Removal of sessile polyp of rectum.
A. Enlarged incision exposing rectum:—*a*. Sessile polyp of rectum, *b*. Incision in rectum for removal of sessile polyp of the rectum, *c*. Sacrotuberous ligament, *d*. Sacrum.
B. First layer of sutures in repair of incision in rectum.
C. Second layer of sutures in repair of incision in rectum and placement of catheters.

during the preoperative and postoperative periods. Enemas containing sulfasuxidine were used as a part of the preoperative treatment.

The patient was placed in the prone position with the head lowered, the pelvis elevated and the thighs lowered and separated. An incision going slightly medially was made on either the right or the left side of the perineum from just lateral to the coccyx to about 3 cm. from the anus into the ischiorectal

fossa. The incision avoided the external anal sphincter and the internal anal sphincter (Fig. 1A). Depending upon the position of the polyp, the coccyx might or might not be removed. The incision was extended cephalad if it were necessary to remove the coccyx. The levator ani muscle was dissected from the rectum. The outer layer of the endopelvic fascia was cut to enter the retrorectal space. The inner layer of the endopelvic fascia was incised (Fig. 1B). The assistant inserted the index finger of the left hand into the rectum and evaginated the rectal wall containing the polyp into the wound. If the tumor was on the anterior wall, the rectum was freed in that area. Occasionally with tumors on the anterior wall, an incision might be made posteriorly and the tumor removed transrectally. The polyp and an adequate amount of surrounding wall of the rectum were excised (Fig. 2A). The incision was closed transversely by an inner layer of interrupted sutures of number 00 chromic catgut with the knots being tied in the lumen. The sutures at either end were used as guides (Fig. 2B). An outer layer of interrupted black silk sutures to invert the first layer of catgut sutures was then placed. The incision may be closed, however, in the most convenient manner since the rectum is large and a subsequent stricture need not be feared. Drainage was provided by two Penrose drains, or better yet, by four catheters brought out through stab wounds. The wound was closed with interrupted sutures of number 00 chromic catgut for the inner layer of the endopelvic fascia, the levator ani muscles and the outer layer of the endopelvic fascia, number 00 plain catgut for the subcutaneous tissue and black silk for the skin. A rectal tube was inserted through the rectum into the lower part of the sigmoid colon and then sutured to the skin around the anus with black silk (Fig. 2C).

The use of air-vent suction of about −20 cm. of water provided by two of the rubber urethral catheters and a Stedman pump and the instillation of varidase afforded greater security at the line of closure in the rectum. Blood and/or pus which may collect in the area and retard healing, are liquefied by the varidase and are removed by the suction. A dry wound heals more rapidly than a wet one.

Case Reports

Case 1:—A 72-year old white man, admitted to the hospital on 11 September 1952, complained of constipation for about two and one-half years, worse in the last month, and bleeding from the rectum for one month. A proctoscopy elsewhere showed a tumor of the rectum and the patient was referred for treatment.

A soft compressible freely movable tumor was felt in the rectum. On proctoscopy, the mass about 5 cm. in diameter with a base about 3.5 cm. in length and about 2.5 cm. in width was felt on the right lateral and posterior walls of the rectum about 7 cm. from the anus. Biopsy of the lesion on 12 September and on 22 September showed a benign rectal polyp.

The roentgenogram of the chest was essentially negative. The barium enema showed an irregular filling defect on the right lateral wall of the rectum but the colon was otherwise negative for definite evidence of pathological changes.

The polyp was removed through an incision on the right side of the perineum on 25 September. A subperiosteal excision of the coccyx was done to facilitate exposure since the tumor was high in the rectum. Two Penrose drains were placed down to the site of closure through a lateral stab wound. A rectal tube was placed through the rectum into the lower sigmoid and sutured to the skin around the anus.

Most of the tissue was composed of polypoid hyperplastic rectal mucosa. Uniform mitotic figures were frequent. Invasion was not present and the cells were not neoplastic. The diagnosis was a benign rectal polyp.

The wound healed by primary intention and the Penrose drains were removed on 30 September. The rectal tube was removed on 1 October. All skin sutures were removed on 4 October. The wounds were healed when the patient was discharged on 8 October.

On 15 January 1953, the wounds were healed. The digital examination of the rectum did not show a mass. On proctoscopy, the mucosa of the rectum was healed and a persistence of the polyp was not seen.

On 8 April the patient was without symptoms. The wounds were still healed. The proctoscopic examination showed a healed wound in the rectum and did not reveal a polyp. The patient did not return for further examination.

Case 2:—A 64-year old white man, admitted to the hospital on 23 June 1953, had a right inguinal hernia present for about seven or eight years, and a left inguinal hernia present for about six months. A considerable degree of constipation was also present.

A large direct right inguinal hernia and a small left direct inguinal hernia were present. A soft sessile polyp about 1.5 cm. in diameter was on the posterior wall of the rectum about 6 cm. from the external anal sphincter.

The roentgenograms of the chest were normal. The barium enema did not show an intrinsic lesion in the colon.

The proctoscopic examination confirmed the size and the location of the polyp in the rectum. A piece of the tumor removed for biopsy showed a benign rectal polyp.

The polyp was removed through an incision on the left side of the perineum on 17 July. A number 16 French rubber urethral catheter was inserted through each of two stab wounds placed laterally into the depths of the main wound.

A rectal tube was placed through the rectum into the lower sigmoid and sutured to the skin around the anus.

The contents of one ampoule of varidase containing 107,000 units of streptokinase and 129,000 units of streptodornase were dissolved in 10 c.c. of physiologic saline. The solution was stored in a refrigerator when not being used. A fresh solution was made daily. Five c.c. of the solution were injected through one of the catheters alternately twice a day from 18 July through 22 July. The catheters were clamped for 4 hours after each injection to permit digestion of fibrin and desoxyribonucleoprotein and then suction of about —20 cm. of water was applied to the wound by a Stedman pump for the next 8 hours. The catheters and the rectal tube were removed on 22 July. All of the skin sutures were removed on 27 July. The wounds healed by primary intention. A herniorrhaphy for a right indirect inguinal hernia was done on 27 July. The patient was discharged from the hospital on 7 August. The patient did not return for further examination.

Summary

Sessile polyps of the rectum are better removed by an external operation since the full thickness of the rectal wall can be excised. Two patients with a rectal polyp have been treated successfully in this manner.

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OBSERVATIONS ON THE DEVELOPMENT OF GASTROENTEROLOGY DURING FIFTY YEARS*

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"We reap what others have sown"—*Fothergill*

"What is life for, if it is not to make it less hard for others."—*George Elliott*

With this theme in mind, I should like in this present writing to pay tribute to the pioneers who blazed trails through the forests of ignorance to bring the light of progress to us. Each has played his part by contributing something to the sum total of human knowledge. Fortunately, life is not a treadmill, but an escalator on which men ascend to certain heights and then pass on to their successors their accomplishments, that they too may reach higher estates.

The purpose of this paper is a simple one. In order to appreciate our own good fortune, it is necessary that we should know something of the life and work of those whose efforts have made the present comparatively easy for us. The following brief chronological data with reference to those who pioneered surgical procedures and physiologic investigations, will sketch in the fortuitous historical background in the development of the surgery of the stomach and duodenum.

Our beginnings are in 1812 when John Archer, an American surgeon, was the first to suture a stab wound of the stomach[1,2].

Following this, in 1837, Egsberg, a Norwegian army surgeon, was the first to suggest the operation of gastrostomy. He justified his suggestion by referring to William Beaumont's case, the half-breed Indian, Alexis St. Martin (1826).

These ventures stimulated a host of new indications.

Watson of New York, in 1844, recommended gastrostomy as a means of prolonging life in cases of stricture of the esophagus[3]. In 1849, Sediliot reported the first gastrostomy deliberately planned and performed upon a human being. This was followed in 1853 when Fenger (Copenhagen) performed the second gastrostomy on man. Then in 1869, Maury (Philadelphia) performed the first American gastrostomy. The operation was done for the relief of a stricture of the esophagus. It was deliberately planned and performed after consultation with Samuel D. Gross, Pepper and Weir Mitchell. The patient died[4].

Two years prior to Archer's work, Dr. John Jones, a native of Philadelphia, performed the first pylorectomy in 1810[5]. It was not until 1877, however, that

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Billroth advocated pylorectomy and partial resection of the stomach based on experimental work which had been done by his assistants, Gussenbauer and von Winiwarter. Billroth's work was so remarkable that Sir Gordon Taylor, one of the great surgical leaders of our time, called him "the real founder of gastric surgery" and Richard Lewison remarked that "The technic of gastrectomy has been changed very little since its conception by Billroth in 1881."

Kroenlein and Mikulicz modified and simplified Billroth's methods and Polya and Reichel later followed the same procedure as Kroenlein. Balfour subsequently modified this method by using the antecolic route instead of the retrocolic route of Polya.

In 1876, Czerny and Kizer performed experimental resections of portions of the stomach in dogs. This was followed by the first resection of the stomach in man in 1879 by Pean. In 1880, Rydigier performed the second pyloric resection in man and in 1881, Billroth reported *the first successful case of pyloric resection.* Three years later in 1884, Randolph Winslow (Baltimore) became the first American surgeon to attempt pylorectomy. He resected the pylorus for a cancer of the stomach at that time.

By now, surgery was ready for gastrectomy.

Conner (Cincinnati) in 1884 was the first to perform this procedure. His patient died on the table from shock. The first *successful* total *gastrectomy* was reported by *Schlatter* of Zurich in 1897. One year later, in 1898, the second successful case was reported by Brigham of San Francisco. Theodore Kocher, however, was the first to perform a total gastrectomy and esophagoduodenostomy on *June 9, 1899.* The patient died[7].

New procedures were now introduced. In 1881, Wolfler was the first to perform a gastroenterostomy. The operation was done for a carcinoma of the stomach. Attention has been repeatedly called to the historic fact that Nicoladoni, an assistant to Wolfler, suggested the operation of gastroenterostomy to his chief in the course of the operation on the patient for cancer of the pylorus.

Rydigier introduced this procedure for the cure of *gastric ulcer* in 1881. He reported that he resected a large ulcer from the posterior wall of the stomach at the same time. A cure was claimed.

In 1882, Czerny performed the same operation. It was not until 1884, that Ransohoff of Cincinnati became the first American surgeon to perform a gastroenterostomy. The patient succumbed after a few hours. In the meanwhile, Courvoissier, in 1883, suggested utilizing the posterior approach for making the anastomosis. Von Hacker, however, is usually credited with the suggestion of making the posterior anastomosis in 1885. He deserves priority for being the first to suture the edge of the rent in the mesocolon to the stomach wall, thus making a distinct addition to the technic of the operation[8].

These procedures were followed in 1892 by gastroduodenostomy, Jaboulay suggesting the operation, which he first performed in 1894. Later on, J. M. T. Finney described and advocated gastroduodenostomy under the title of pyloplasty in 1902 at a meeting of the American Surgical Association.

Now that gastroenterostomy was an established procedure, modifications of technic were being advanced. It was recognized very early that a gastroenterostomy in the presence of a patent pylorus was ineffective. Various methods for obliterating the pylorus with suture, passing around the pylorus with a piece of tape or fascialata and even a more radical method of obstructing the pylorus, was adopted by von Eiselberg in which the stomach was severed from the duodenum and both ends closed with suture. The infolding with sutures for obliteration was commonly known as the Kelling-Mayo method. The rationale of obliteration of the pylorus was that if it remained patent, the gastroenterostomy stoma would not function.

The annoying and persistent postoperative vomiting which followed the long loop operation led to discussion of whether the anastomosis should be made isoperistaltic or antiperistaltic. It also led to the use of an enteroanastomosis. The enteroanastomosis was made with either a Murphy button or by the suture method. Both of these technics were in use by Professor Matas in his clinic as late as 1907 to 1910.

Dissatisfaction with gastroenterostomy on the part of some led a great many outstanding surgeons, notably Sir Berkeley Moynihan, as early as 1919, to report that he had "abandoned gastroenterostomy alone in the treatment of chronic gastric ulcers".

Lewison in 1925 expressed the opinion that "the enthusiasm for gastroenterostomy will wane during the next few years and that in ten years gastroenterostomy will be used for the treatment of pyloric and duodenal ulcers as a make-shift operation, not as a method of choice. Partial or total gastrectomy should be the method of choice in the surgical treatment of gastric and duodenal ulcer".

The fluctuating opinion on this subject was reflected in an editorial in the Journal of the American Medical Association[9]:

The Choice of Operation for a Duodenal Ulceration. "The problem remains as to what operation should be performed for duodenal ulcer. The medical profession would welcome more accord among authorities on this question".

Frank Lahey, Ravdin and many others have within more recent years given directives based on extensive personal experiences. Lahey remarked in 1942, that "gastroenterostomy is not an operation to be routinely applied for the surgical treatment of peptic ulcer. It is more generally agreed that subtotal gastrectomy is followed by fewer recurrent ulcers and a better digestive state than

results from other less radical surgical procedures." Ravdin stated ten years later, "The therapy of gastric ulcers should be regarded primarily as a problem for the surgeon, provided the surgeon is sufficiently able and experienced in gastric surgery to perform a radical gastric resection with small operative risk."

By now, surgery had advanced far enough so that this procedure could more readily be used in resolving the problem of whether a benign ulcer of the stomach could change its character and become malignant.

This question of whether a gastric ulcer remains throughout its course a benign lesion or whether carcinoma may be grafted upon it has been a moot point through the years. Dogmatic statements had frequently been made that "the leopard does not change its spots" and equal statements have been made, that every ulcer must be looked upon with suspicion as a possible forerunner of malignant disease. These entirely opposite points of view had led to confusion and in some instances to disaster. Those who had been suspicious of every ulcer of the stomach were doing many needless radical gastric resections, while those holding the opposite point of view were responsible for failure to recognize the disease early enough to allow for a cure. Reliance on skillful technic, transfusions, improved anesthesia and antibiotics, had by now encouraged a bold and rash attitude which was not justified by the code which should guide our professional activities.

Kelley and Larrimore in 1954 lamented the lack of unanimity regarding the therapeutic approach. They expressed the opinion that "the uncomplicated gastric ulcer should not be removed in order to prevent the development of cancer. A *gradual unanimity of opinion among pathologists has developed*". They believed that "the gastric lesion is either benign or malignant from its inception. Cancer does not arise in a preexisting gastric ulcer. There is then no reason to resect benign ulcers as a means of preventing later development of cancer".

As at present, Ralph Brown and Bockus are in full accord with that expressed opinion. Brown states, "I firmly believe that clinical experience in future years will free gastric ulcer from the malignant suspicion in which it is now held by many medical men" and Bockus in 1952 stated "malignant degeneration does not occur in gastric ulcer as often as had been anticipated". Shields Warren has likewise concurred by stating, "there have been only four cases in which evidence was found that cancer probably arose on the basis of preexisting benign gastric ulcer".

An entirely opposite view, however, was expressed by Marshall when he reported 411 consecutive cases of gastric ulcer, in which resection had been performed. *He noted an incidence of 15.8 per cent malignancy in this group* and he concluded, "it is our opinion that a higher percentage or more of gastric ulcers should be resected, since an appreciable number have been found at operation to be malignant. *Temporizing with nonhealing ulcerating lesions of the stomach involves serious risk to the patient and is completely unjustified.*"

Ravdin has emphasized, "the difficulties experienced by the surgeon and pathologist in differentiating between the benign and malignant lesion".

And so the argument goes on. Not only as to who should treat the patient, and whether the gastric ulcer may become malignant, but whether the ulcer is primarily malignant.

If one moralizes on this subject, he is forced to conclude that no formula, no short cut and no rule of thumb should be adopted. The need for careful analysis of the clinical manifestations, a proper evaluation of all laboratory data, the avoidance of a pontifical attitude but, on the contrary, an approach to the problem with a dash of humility is the duty of every conscientious surgeon.

It is worth remembering that even reports by pathologists are questioned by equally expert men in that field.

The evolution of gastroenterology from medical and surgical standpoints has been extremely rapid. Those of us who were introduced to the study of medicine 50 or more years ago were not familiar with the word gastroenterology. Those who doubt this statement will be convinced by consulting the Oxford dictionary or Webster's dictionary published as late as 1921. Gould's medical dictionary published in 1903 does not contain the word. In later editions, Gould has kept up with the development of the specialty and defines the term. This does not imply that the subject of gastrointestinal disease did not interest the profession but, it does mean that the definite specialty had not been "dissected" away from the parent—internal medicine. Actually, the great names in the literature of the early part of the twentieth century, Sippy, Einhorn, Smithies, Thomas Brown, Friedenwald, Ralph Brown, Rehfuss, etc., who were leaders, were styled internists. In the rapid growth of scientific knowledge of specialized character, individuals began to be extremely jealous of their own province. Hospitals had great difficulties in their efforts to satisfy various groups with reference to the allotment of cases. I should hasten to add that this did not apply only to the differences of opinion among internists of various shades, as surgeons have watched the gradual "epilation" of what was once general surgery until at the present time it does not have even the naked form. I started to say the bones are not left for the general surgeons to "gnaw" on. I find that even that particular field has rather rudely been confiscated by orthopedists and bone and joint surgeons.

When recording progress during the past 50 years, it is important to recall that surgery was in its swaddling clothes when some of us were introduced to medicine. The development of the x-ray, improvement in anesthesia, aseptic methods, changing physiologic concepts, the widening horizons of biochemistry, chemotherapy, antibiotics and the gradual unfolding of knowledge with reference to the endocrine system, replacement therapy and transfusions have all contributed to advancement, understanding and approach to the subject under discussion.

During that same period, an entirely new vocabulary has developed, particularly along the lines of psychosomatic investigations. Parenthetically, I might say that some of the newer words on a printed page have as much meaning to some of us as a foreign language.

Fifty years ago when medical students were introduced to the pneumogastric or vagus nerve, attention was directed to its wandering character. We are indebted to Dragsted for the more recent developments which are being made use of to curb the action of the "wanderer". As a matter of history, the vagus nerve has been implicated as a cause of hypersecretion in the fasting stomach for more than 70 years.

In 1885 Beynard and Loye[9], performed a conclusive experiment in the case of a criminal who had suffered capital punishment. They stimulated the vagus nerve 45 minutes after death had occurred and were able to cause a secretion of gastric juice in the stomach.

The classic experiments of Pavlov and Schumowa[10], demonstrated abundant secretion of gastric juice in experimental animals which had both a blind esophageal pouch and a stomach fistula. *If the vagi were severed, a secretion of gastric juice did not occur.*

With the foregoing as an introduction, one might say that in the history of the development of gastroenterology there are two outstanding factors:

1. The greatest single factor in the development of our knowledge of intrinsic gastrointestinal diseases has been the x-ray discovered by William Konrad Roentgen in 1895.

2. The appreciation of the need for cooperation and coordination of the efforts of physicians and surgeons.

In recent years many have stressed the importance of the coordinate and cooperative problem of surgeons and gastroenterologists in the effort to solve the common problem—What is the best approach and what is the safest procedure for the individual case?

In so broad a subject as the one I have chosen, it is necessary to fix a particular date and to use that as a sign post. Fortunately, such a date is easily found. In 1922, a symposium was held in a joint session of the Sections on Surgery and Gastroenterology at a meeting of the AMA, to discuss the relative value of medical and surgical treatment of gastric and duodenal ulcers. Sippy, Frank Smithies, Thomas R. Brown, Arthur Dean Bevan, J. M. T. Finney, A. J. Ochsner, W. C. Alvarez, Shelton Horsley, Seale Harris and Charles H. Mayo participated.

Thomas R. Brown summarized the situation from the medical man's point of view admirably—

"In presenting one's views as to the relative value of nonsurgical treatment of gastric and duodenal ulcer, one cannot help feeling the essential and inherent difficulties of such a discussion. The enormous amount of literature on this subject of the past few years, with many conflicting articles trying to evaluate the various modes of therapy all show beyond peradventure the unsatisfactory and unsettled state of this subject, and how much brave physicians and surgeons are in need of some rational basis of agreement as to the proper mode of attack in this group of cases".

"We are still waiting for a Moses to lead us out of the wilderness. That form of therapy must be employed, which is best suited to the special needs of the patient, and this can only be brought about by a closer cooperation between the clinician and surgeon: *then we shall no longer talk of medicine versus surgery, but medicine and surgery in the treatment of gastric and duodenal ulcers*".

Dr. J. M. T. Finney in discussion during this symposium stated: "It must be admitted that the prevailing feeling is one of dissatisfaction with both medical and surgical treatment. I have tried every accepted method of surgical treatment and I am still dissatisfied with the results".

In approaching this same subject at the Fifth Annual Convention of the National Gastroenterological Association in New York in 1940, I stated:

"It is generally accepted that in almost all conditions, cooperation between the surgeon and various specialists who refer patients to him is essential. Ideas have changed with increasing information with reference to duodenal and gastric ulcers. One of the most important problems involved in many of these cases is the question—when is a case medical and when should it be referred to the surgeon. It is true that in most instances the physician (gastroenterologist or internist) is the first to see the patient with ulcer and it devolves upon him to make the diagnosis, to decide on how long he should proceed with the treatment and when to call the surgeon in consultation.

"It must be conceded that if surgery is to be applied, it must be done at an opportune time and adequate skillful surgery performed. If these two maxims are overlooked, dissatisfaction is bound to follow. Proper medical follow-up is essential in order to obtain for the patient the ultimate which he desires, that is, comfort, if not cure. Surgeons should not approach any problem by the rule of thumb. The surgeon should select that procedure which most nearly meets the margin of safety in the particular patient".

At that time, I summarized my feelings as follows:

"The problems which confront us today may be compared to relay races, each participant does his best up to a certain point and then cheerfully relinquishes the struggle that others may carry on. It becomes increasingly important for us to fix, for the guidance of others who are to follow us, rational

lines of procedure so that our mutual problem, the patient, may obtain that which he seeks, a restoration of health and economic efficiency".

Let us now refer to the first of the two aforementioned factors in the development of gastroenterology.

Until the discovery by Roentgen, the profession was forced to depend upon a formula which was repeated almost verbatim by most authorities of that period.

Austin Flint[11] stated, "The diagnosis of gastric ulcer may be made with much certainty, providing that diagnostic symptoms be present, namely, pain of a burning or gnawing character, limited to a circumscribed space in the epigastrium, with tenderness, the pain felt directly after ingestion of food and especially after certain kinds of food. Vomiting occurring during the process of stomach digestion and followed by relief and finally gastrorhagia or hematemesis".

Prior to the use of the x-ray, the only available diagnostic procedures other than the clinical examination and palpation of the tumor and other associated evidences of a late stage of the disease was the use of gastric analysis.

Clinicians developed tubes (Jutte, Einhorn, Levin, Rehfuss and others), string tests and even artificial distention of the stomach with carbon dioxide gas. Great reliance was placed on gastric analysis. It is true that many pioneers in the field of radiology began to demonstrate the great usefulness to which the x-ray could be put. Hemmeter in 1906 first demonstrated the presence of a mass or crater and Haudek in 1910 coined the expression "niche". Bockus claims that Haudek "placed the roentgen diagnosis of ulcer on a substantial basis".

As early as 1913, Mills and Russel Carman lamented the fact that European investigators have endeavored to increase the accuracy of gastrointestinal diagnosis through the aid of the roentgen ray and that the method which gives "promise of such an advance in methods of diagnosis which owes its origin to Cannons", should have awakened in this country so little interest as compared to that evidenced by German and English clinicians and roentgenologists.

"*Little has been done in our country in the way of confirmation of the work already done or towards familiarizing us with an already voluminous literature.*"

Carman's work was recognized by Sir Berkley Moynihan in the following words: "I have relied upon my colleague, Mr. Scargill. His method which follows so closely upon those of R. B. Carman of the Mayo Clinic, shows that the possibility of making an accurate diagnosis in gastric ulcer is greatly increased by the x-ray examination. Indeed the radiographic examination alone is more accurate than all other methods combined.

"The radiographic method is the one certain method of diagnosis and *is now an indispensable addition to the older and far less accurate procedures*".

The classic work of Carman, George Pfahler and Gregory Cole in the United States, did much to develop the appreciation of the profession of the value of the x-ray mode of diagnosis. Even the enlightenment gained by the use of the x-ray was doubted by many.

Sippy, in discussing Pfahler's paper in 1916 stated: "I wish to supplement the doctor's plea by making a plea for complete examination, nonroentgenologically. By working with a little understanding, there are mighty few cases that cannot be studied without roentgenology and conclusions drawn that will be influenced very little by roentgenology. From long experience, it is possible to do our work so accurately, that it is only now and then that the roentgen ray will give you any material advantage".

Dr. J. Guttman of New York participated in the discussion of Pfahler's paper and he stated: "If I were to choose my method of diagnosis, I would say give me clinical experience. If my clinical experience teaches me that I am dealing with a gastric ulcer and laboratory findings tell me that there is achylia and other evidence present which might indicate carcinoma, *I shall be firm in my diagnosis of gastric ulcer.* Often the roentgen ray leads in the proper direction. The failures are not so much because of the ray itself, but because of the way it has been used. *It depends entirely on the man and the method used and on the interpretations of the findings. Taking it as a whole, first comes proper clinical diagnosis, then the laboratory work, whether it be chemical or roentgen ray, done in the proper way and by an expert*".

Carman had in 1913 pointed out some of the difficulties inherent in the use of the x-ray. "The clinician is deficient in knowledge of x-ray technic and the roentgenologist is at a great disadvantage because of his lack of anamnesis of methods of abdominal physical examination and of alimentary physiology. *The only rational solution of the problem is the cooperation on the part* of the clinician and roentgenologist in the utilization and development of the method. It is in this alone, it seems to us, lies the solution and attainment of valuable results".

The pioneer work of Carman begun at the Washington University at St. Louis and continued until his untimely death, when a member of the Mayo Clinic at Rochester, will remain as a classic milestone in the development of the present status of diagnosis of gastrointestinal diseases which were obscure and the diagnosis of which could only be guessed at prior to the introduction of the x-ray. The diagnostician and surgeon owe in large measure their present advanced status in the management of gastrointestinal conditions to two factors:

1. The development of a knowledge of the x-ray and

2. An appreciation of the necessity for coordination of all information available and cooperation on the part of surgeons and gastroenterologists.

If the present generation can add as much as our immediate predecessors, we can count ourselves fortunate.

The deadly leaves of autumn are but the forerunners of the green sprigs of spring. A life is given that the future may be better. We should know the past that we may appreciate the present and have a hopeful outlook for the future.

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LIGATION OF THE HYPOGASTRIC ARTERIES AND ITS COMPLICATIONS IN RESECTION OF CANCER OF THE RECTUM*†

R. VENANCIO TAJES, M.D., F.A.C.G.

Montevideo, Uruguay

Resection of the rectum is a major surgical operation and hemorrhage during the operation or immediately following it may be a serious complication. This complication does not seem to be so serious in the abdominal stage providing that proper ligation of the arterial supply to the parts is done. It seems to be in the perineal phase of the operation that the patient is most severely shocked due to a sharp loss of venous blood, combined with tension on the rectal nerve supply having its roots in the sacral plexus. Blood transfusions and the infiltration with novocaine of pararectal tissues seem to reduce considerably the probabilities of operative shock.

Arterial hemorrhages due to the section of the middle and inferior hemorrhoidal arteries are easily stopped by means of ligating the vessels involved but venous hemorrhage is more difficult to control and is a prime factor in causing shock.

In an effort to avoid as much of this venous shock as possible, we decided to perform bilateral hypogastric arterial ligation in the abdominal stage of the operation and we are reporting on two cases in which an excellent hemostatic result was thereby obtained. In one of the cases, however, serious complications resulted despite the fact that such complications are extremely rare as indicated by a review of the literature and of the history of this surgical procedure over the past fifty years.

Ligation of the hypogastric artery was first reported by Stephens of Vera Cruz in 1812. This operation was done for the treatment of an aneurysm of the gluteal artery and was done extraperitoneally. Another case of aneurysm of the gluteal artery was reported by Haggard who stated that unilateral hypogastric ligation successfully managed the situation and, who mentioned that Könisberg had collected 45 cases prior to 1907.

Baumgartner in 1888 employed bilateral ligation of the hypogastric arteries for the first time in the case of inoperable carcinoma of the uterus. Jean Louis Faure, the French gynecologist, recommends in his textbook that bilateral hypogastric arterial ligation be done when ligation of the uterine arteries offers unusual difficulties. Faure advises that the ureters must be carefully identified and observed in order that inadvertent damage to the ureters be avoided. Other authors, such as Monod, and Sobre Casas, in well known textbooks, mention the

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†Revised by James A. Ferguson, M.D., F.A.C.G.

advantages of bilateral hypogastric ligation but do not mention any of the serious complications which can result.

In 1898 Quénu and Duval described the surgical technic as follows:

"About 3.5 centimeters from the medial line, a 4 centimeter incision is made in the peritoneum. This incision is parallel to the vessel line, the middle part of which corresponds to the promontory of the sacrum. The edges of the peritoneal incision are retracted by using a probe. The external edge carries the ureter which is set free in this way. In this peritoneal hole we observe the common iliac artery in the upper angle, bifurcation in the middle, and in the lower angle we find the external and internal arteries joined and still covered with fascia. This sheath is incised according to general technic, the internal iliac artery is exposed to view and picked up from within out."

Leventhal, Lash and Grossman reported in 1938 a series of 5 patients in whom bilateral ligation of the hypogastric arteries was performed as part of the surgical resection of carcinoma of the cervix. These authors mention no complications. Salzberg, Allen Fuller and Hoge have recently reported a series of six patients in whom bilateral hypogastric artery ligation was done as part of the operative attack on carcinoma of the uterus.

Though frequently mentioned in gynecology reports, bilateral hypogastric ligation is seldom seen in proctologic or general surgical reports in reference to resection of the rectum. If difficulties in pelvic dissection seem to indicate that the procedure should be done, and this is not often, it is well to know that it can be done though there is some calculated risk.

Chalier and Mondor in their textbook on "Cancer of the Rectum" state that Quénu operated on a 50-year old woman for cancer of the rectum in 1896. At that time Quénu performed the operation in two stages with a six-day interval between the abdominal and perineal stages. This very operation with some modifications was popularized by Ernest Miles some years later and is now part of our standard armamentarium. Quénu at that time recommended that the operation be done in following steps:

1. Midline incision of the abdomen.

2. Ligation of the hypogastric arteries.

3. Liberation of the sigmoidcolon after a left colostomy is made.

4. Rectal liberation and opening of the peritoneal "cul de sac".

5. Perineal resection of the rectum approximately a week following the above steps.

Hartman, in his well known textbook on surgery of the rectum, abandoned Quénu's technic as being unnecessary and time consuming.

Brown Keyes has drawn attention to the investigations of Wright and Shafiroff, in the Department of Experimental Anatomy at New York University Medical School, on the subject of collateral circulation involved following ligation of the hypogastric arteries. These authors performed a bilateral hypogastric ligation on a cadaver and then injected a radio-opaque medium into the abdominal aorta, well above the origin of the inferior mesenteric artery. X-ray studies of the injected specimen revealed an excellent perineal circulation which was obviously produced through the collateral vessels.

According to Shafiroff, the collateral circulation following bilateral hypogastric ligation consists of the following vessels:

1. The uterine artery branching from the hypogastric artery anastomoses with the ovarian artery which is a branch of the aorta.

2. The middle hemorrhoidal branch of the hypogastric artery anastomoses with the superior hemorrhoidal artery coming from the inferior mesenteric. The middle hemorrhoidal also anastomoses with the inferior hemorrhoidal which is a branch of the internal pudendal artery which again is a branch of the hypogastric artery.

3. The obturator artery branching from the hypogastric artery gives off pubic branches which anastomose with the inferior epigastric arteries coming from the external iliacs.

4. The inferior gluteals from the hypogastrics anastomose with the circumflex and perforating branches of the deep femoral artery.

5. The superior gluteals from the hypogastric anastomose with the lateral sacrals and thence with the middle sacral artery.

6. The ileolumbar arteries from the hypogastric anastomose with the lumbar arteries from the aorta.

7. The vesical arteries which supply the bladder are both branches of the hypogastric artery and they anastomose with the uterine arteries also from the hypogastric and with the vaginal arteries.

According to the foregoing investigation of collateral circulation upon which ligation of the hypogastrics would depend, such collateral is completely adequate and there should be no serious trouble in ligation. These troubles do exist, however, and may be of a serious consequence. Shafiroff's investigations coincide nicely with those stipulated by Gray which are as follows:

"The circulation after ligature of the hypogastric artery is carried on by anastomoses of the uterine and ovarian arteries; of the vesical arteries of the two sides; of the hemorrhoidal branches of the hypogastric with those from the inferior mesenteric; of the obturator artery by means of its pubic branch with the vessel of the opposite side and with the inferior epigastric and medial

femoral circumflex; of the circumflex and perforating branches of the *profunda femoris* with the inferior gluteal; of the superior gluteal with the posterior branches of the lateral sacral arteries; of the ileolumbar with the last lumbar; of the lateral sacral with the middle sacral; and of the iliac circumflex with the ileolumbar and superior gluteal."

From a theoretical point of view then, collateral circulation following bilateral hypogastric ligation appears to be efficient. The circulation, however, may fail and necrosis phenomena due to ischemia may occur. Fortunately, these accidents are uncommon but if they do occur, the result is invariably serious and might even be fatal.

A similar problem is now being discussed pertaining to the ligation of the hepatic artery as a treatment for cirrhosis of the liver.

In 1925 Finaly reported a carcinoma of the rectosigmoid removed by segmental resection and primary anastomosis of the iliac colon to the distal rectum. Prior to the pelvic dissection bilateral hypogastric ligation was done. A few days after the operation, necrosis of the scrotum appeared and this process spread little by little over the perineum, the perianum and both ischiorectal fossae and the patient died on this 16th postoperative day. Finaly also reported at that time the case of a 76-year old woman in whom a Wertheim operation for carcinoma of the cervix was done and bilateral hypogastric arterial ligation was a part of the operative technic. A week after the operation, despite the fact that preoperative cystoscopy was normal, an uncontrollable hematuria occurred. Two weeks later a large flap of tissue was eliminated through the vagina. This tissue was found to be necrosed mucosa of the bladder with the attached urachus. This patient, however, survived and was discharged a month postoperative with a permanent vesical fistula.

The following case in which we performed bilateral ligation of the hypogastric arteries to avoid operative bleeding confirms the experience of Finaly.

Case Report

M. J. P., a Brazilian woman, 58 years of age was admitted 26 June 1954, complaining of rectal troubles which had begun in October 1953, abdominal pain which appeared suddenly and which became stronger during defecation, and constipation alternating with diarrhea. There were infrequent bloody and purulent discharges through the anus. Tenesmus and dysuria were severe. There was some loss of appetite and loss of weight and the patient complained of abdominal distention, improved by passing of gas per rectum. The patient's last menstrual period had occurred ten years prior to admission.

Clinical Examination:—The patient was a well developed female appearing to be in good general condition. Abdominal examination was negative except for a slightly enlarged liver and a palpable liver edge. The remainder of the

physical findings were normal except for digital rectal examination which indicated a palpable firm lesion at fingertip on the anterior ampullary wall. Proctosigmoidoscopy confirmed the impression of the rectal tumor and a small rectal mass on the anterior abdominal wall was biopsied. The pathology report showed characteristics of a malignant, ulcerative, infected and purulent adenoma.

Laboratory Studies:—Blood urea: 0.25 gm. per cent; blood sugar: 1 gm. per cent; plasma proteins: 7.85 gm.; red cells, 4,750,000; white cells, 4,250; Platelets: 274,640; Hb. 118 per cent; blood clotting time: 7 minutes; bleeding time: 1 minute.



Fig. 1



Fig. 2

Fig. 1—Appearance of the necrosed areas after the partial resection of the left *gluteus maximus* muscle and of the skin.

Fig. 2—Appearance of the necrosed areas two months after the operation. We can observe the scar on the left cutaneous zone.

Operative Procedure:—On 10 July 1954, combined abdominoperineal resection of the rectum was done through a midline incision extending from the symphysis to a point slightly above and left of the umbilicus. The abdomen was systematically explored and no abnormalities were seen in the peritoneal cavity, in the liver, gallbladder or stomach. Both hypergastric arteries were ligated without difficulty, the ureters being identified and spared. After novocaine infiltration of the presacral plexus both lateral ligaments of the rectum were cut without hemorrhage. The left ovarian artery was cut

and tied to separate the sigmoid colon from the left adnexa. Presacral decollement was done, the sigmoidcolon divided and the distal end covered with a sterile rubber glove and tucked into the presacral hollow. The pelvic peritoneum was closed incorporating the adnexa and the uterus and a definitive left colostomy was constructed. The abdominal wall was closed in layers. The perineal portion of the operation was done quickly and without incident and drains were placed in the perineal wound.

Postoperative Course:—The patient's postoperative course was very smooth and uneventful for six days, at which time two large phlyctena appeared on

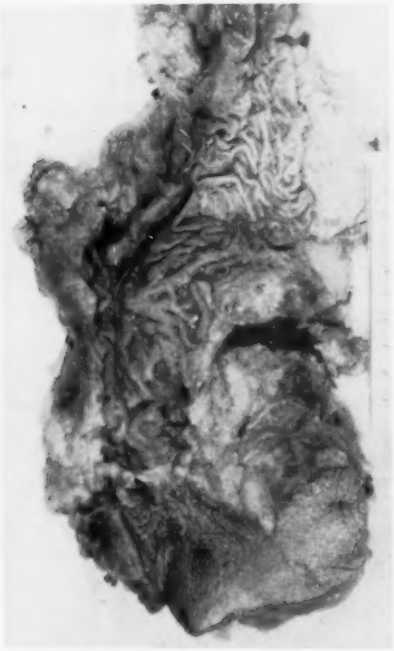


Fig. 3—Operative specimen where the anorectal cancer described before (Clinical History 4070) can be observed.

the buttocks (Fig. 1). On that day the urinary catheter was removed and slight vulvar edema was noted. Four days later, the patient's tenth postoperative day, a necrotic area was observed on the right buttock a little above the operative wound. The posterior wound had opened because of inadequate healing. On the left edge of the wound was a large necrotic area involving not only the skin edges but also gluteus maximus muscle. The area seemed to be that supplied by the superior gluteal artery from the left hypogastric.

The necrotic tissue was completely debrided and the resulting defect treated with ultraviolet rays and cod liver oil pads. The appearance and condition of the wounds improved very slowly (Fig. 2).

Colostomy function was at all times normal but a small fecal fistula developed at the medial border of the colostomy necessitating surgical intervention.

In spite of these complications, the patient's condition improved gradually and at the time of this writing she is in the best of health. Plastic revision of the wounds was necessary.

Pathology Report on Operative Specimen:—The specimen consists of a piece of large bowel about 20 cm. in length which shows a tumor above the anal outlet. Microscopically, this tumor is a cancerous ulcer (infiltrating and scirrhous) with polyhedral and atypical cells (Fig. 3).

Clinical Summary and Comment:—This is a case of anorectal cancer for which a combined abdominoperineal resection of the rectum was done. Bilateral hypogastric arterial ligation in the abdominal phase of the operation was done to provide maximum hemostasis. This technic served its purpose well as the posterior or perineal phase of the operation was practically bloodless. A delayed necrosis of the buttocks, however, in the areas supplied by the superior and inferior gluteal arteries, occurred several days following operation.

From a review of the literature available, we have deduced that this complication is not very frequent, since there are only two published cases which we have been able to study. Despite the opinion of authors such as Faure, Kirschner, Zenker, and Quénu, that the procedure does not cause any subsequent trouble to the patient, we are convinced that ligation of the hypogastric arteries is not completely harmless and that in a small number of cases it may cause serious trouble. Nevertheless, we do not think that the procedure should be abandoned. The technic can be used when hemostasis is difficult and danger of a serious hemorrhage threatens and it can be used without fear of serious complications in the majority of cases.

TOXIC REACTION TO MILTOWN (EQUANIL)

L. CRISMON, M.D.

Lewiston, Idaho

Case Report

In as much as 2-methyl-2-n-propyl-1,3-propanediol dicarbamate-(Equanil) or (Miltown) is being used with increasing frequency for anxiety and tension states as well as other conditions, it would seem appropriate to report an additional toxic reaction.

Case Report:—Mr. H. K., white, male, age 42, was seen because of a continuation of rectal pain of 5 years duration and after 4 rectal operations. These included drainage of fistula, hemorrhoidectomies, fissure repair, and re-repair. The last being 1 month ago. In addition to the chief complaint he had upper abdominal trouble of an ulcer-like nature that would come only when he had been having prolonged rectal pain. The patient had had an urticarial reaction to penicillin on one previous occasion and had fainted following a caudal block with novocaine; however, he had known of no purpura at any previous time in his life nor had he had any spontaneous diseases suggestive of this. No history of asthma, or hay fever, or urticaria other than from penicillin. The patient recently has been in quite an anxious and tense state. It was believed that if the tension could be relieved some it would favorably influence the course of his rectal healing. On this basis he was given Equanil, 400 mg., 3 times a day.

After the third tablet the patient began noticing eye-smarting and itching. Throughout the night his symptoms increased and by morning he was greatly swollen, could not open his eyes, had mild pruritus, 102° temperature, and general malaise. He was taking no other medicine at this time.

He was admitted to the hospital the next day where examination revealed generalized erythema and edema. There was a petechial rash, rather extensive, over both legs and lower abdomen and to a very slight degree of the upper extremities, a large ecchymotic spot on the right wrist and between the fingers of both hands. He was placed on cortisone and Chlor-Trimetron Maleate. The fever and the reaction subsided over the next 36 hours and he was sent home on a regime of steadily decreasing cortisone dosage.

Laboratory Work:—Showed a normal blood count, no elevation of serum bilirubin, normal platelet count, normal bleeding time, normal clot retraction time, normal clotting time. Tourniquet test was very positive in one minute.

Summary

A case of *purpura simplex* and toxic erythema following the use of Equanil (Miltown) is presented.



President's Message

Looking Ahead

The accomplishment of the aims and objectives of any organization are dependent upon the intelligent cooperation of its officers, committees, and the rank and file of its membership.

This applies to all of us because we are interested in the success of the American College of Gastroenterology, not only now but in the future.

The better understanding we have of our respective offices, the better will be the results of our efforts. Therefore, I feel all attendant responsibilities should be thoroughly spelled out. The same definition of responsibility should apply to all of our committees. One of our most important committees is the Membership Committee. Here, I feel, the responsibility should be distributed from the Governors on down to the grass roots. By that I mean more importance should be given to the Associate Fellows and the Members. This should lead to a uniform expansion of our College.

Our foreign members should be encouraged to greater participation in College activities. They should be made to feel they are an integral part of our organization. They should be on committees and have Governorships.

Finally, we should be sincere, cooperative, and understanding in our daily association with Doctor-members of other organizations in our field. We must sell our purposes and objectives more; and the need for our group in Medicine to others. We must prove we are not at cross-purposes with other gastroenterological organizations but that we are needed in the field where others do not thoroughly reach.

If we can accomplish these aims, the coming year should be one of satisfaction for the new president and his officers.

Arthur A. Kirchner

In Memoriam

ELIHU KATZ, M.D., F.A.C.G.

(1889-1956)

Dr. Katz had the strength of character and devotion to duty that make a physician great. He was one of the founders of the National Gastroenterological Association and of the American College of Gastroenterology and he served as our treasurer for a score of years. The American College of Gastroenterology was his first love and to each of us who knew him, and to the College his loss



can never be replaced. Our institution, the American College of Gastroenterology, is the lengthening shadow of this great man.

JAMES T. NIX, M.D., F.A.C.G.

Elihu Katz, M.D., will be remembered as a quiet unassuming gentleman who was very effective in accomplishing his desires in engineering the financial

affairs of our organizations. He was able to do this, with the rare ability of having everyone love him for it. Our organizations have always been solvent under his guidance. He has built well and the man who is to assume his work will find it easier because of his genius. We are all grateful to Elihu for all he has done for us. May God give us the ability to carry on as Elihu would have it. We will always miss this lovable gentleman who moved so quietly among us.

ARTHUR A. KIRCHNER, M.D., F.A.C.G.

I had the privilege and pleasure of knowing Dr. Elihu Katz for many years. I shall always remember him as a gentleman at all times, even under unusual circumstances. He was quiet and never showed his temper. His ability was unquestioned in the handling of the financial affairs of the organization. Professionally he was well liked by his patients for his kind and understanding ability.

FRANK J. BORRELLI, M.D., F.A.C.G.

We have lost a kindly and devoted member and officer who conducted himself and his office with sincerity and dignity. He was a pillar of strength in our organization. He endeared himself to all who knew him by his cheerfulness, kindliness and friendliness. His courage was outstanding. In his last years, realizing that he was a very sick man, he nevertheless travelled to distant parts of the country to attend meetings of our organization to give us the full benefit of his wise counsel.

JOSEPH SHAIKEN, M.D., F.A.C.G.

It was my pleasure to be associated with Dr. Elihu Katz in the past few years and it is with deep sorrow that we have lost a good friend of the American College of Gastroenterology. He served the College well, as our Treasurer for many years. It was always a pleasure to talk with Dr. Katz and to be associated with him at our Medical Conventions. We have lost one of the important pillars in our college who will be hard to replace. . . .

THEODORE S. HEINEKEN, M.D., F.A.C.G.

It was with deep regret that I learned of the passing of our illustrious, and much beloved Treasurer. We will miss, very much, his friendly smile and his kindly, guiding advice from now on in our Board meetings. His tremendous love, and intense interest in the success of our College will be most difficult to duplicate. It will be very hard for his successor to fill the niche so ably held by Dr. Katz. It has been a most valued, personal privilege to have known him for

the many years during which we were associated together, and to have profited by his splendid example.

Every member of the past Boards will recall how ably and how simply he carried on, that we might understand the intricate problems of a financial program.

We shall always respect Elihu Katz, and what he stood for in medicine and, particularly, what he represented in our great College.

LYNN A. FERGUSON, M.D., F.A.C.G.

It is with profound sorrow that I am penning these few words in memory of my dear and beloved friend Dr. Elihu Katz, whom I have known since the first days of my medical practice. There are no words to express my feelings and sorrow.

Elihu Katz was above all a warm human being, considerate in his personal relations, and understanding. His passing leaves a gaping void in the lives of many. He possessed a striking capacity for public service and was endowed with an original and penetrating mind and was thoroughly grounded in the knowledge of his specialty, gastroenterology, and medicine. Such a life cannot be measured by years alone. Into his brief span he crowded ideals, devotions and achievements which would have done honor to a career twice as long. He maintained a lively and continuous interest in the events of the day, devoured the periodicals and books that were his habitual reading, discussed with his usual keenness the issues and problems that were his customary concern. His death was a great misfortune, and will be a great loss to the New York Academy and the American College of Gastroenterology.

WILLIAM C. JACOBSON, M.D., F.A.C.G.

To say that the saddening news of Dr. Katz' death came as a surprise or shock would be inaccurate, because those of us who were fortunate enough to be with him at the regional meeting of the College in New Orleans last April saw the countenance of a sick and tired gentleman. I shall never forget the enthusiasm and pride with which he rendered the financial statement of the College and so proudly presented a substantial improvement in the College's financial status. This was truly a reflection of his devotion and untiring interest in our organization. It should, and I am certain it will, serve as a stimulus and inspiration to the present and future officers and members of our organization to strive in our efforts to emulate his footsteps.

Although ill and obviously under strain, Dr. Katz at our last regional meeting made it a point to attend our scientific sessions and social functions; here

again with all the attentiveness of his fellow officers he enthusiastically listened to our presentations and discussions. At the social functions, he partook of all the wining, dining and hilarity with the genuine *joie de vivre* just as that of the youngest neophyte.

These remarks, I feel, sketch the personality of a beloved gentleman whose death is a great loss to our College, realizing of course, that they are mere chit chat as compared with the deep wound that his passing has caused his wife. However, I think that these words as well as the many statements of praise that will appear in this issue of the Journal will in some way serve as solace to his dear ones.

His was truly a job well done.

LOUIS OCHS, JR., M.D., F.A.C.G.

The death of Dr. Elihu Katz was a profound personal loss of not only a colleague but of a true friend. We were associated in the American College of Gastroenterology, on the staff of the Department of Gastroenterology at the New York Polyclinic Medical School and Hospital and in many organizations to which we both belonged. Dr. Katz was a kind, generous human being interested in many projects for the betterment of mankind in general and for the improvement of medical education.

When any worthwhile organization appealed to him for support, Dr. Katz was ever ready to give that support with every resource at his command. He gave freely to charitable organizations and expended much of his time and effort heading committees and serving on them, never refusing when asked and often volunteering before he was asked.

In my many years of association with Dr. Katz, he was always a warm, kind, loving individual for whom no task was too great. His friendship was one which I will ever cherish and his passing leaves a great unfilled void.

My sincerest sympathies to Mrs. Katz and the other members of his family.

SAMUEL WEISS, M.D., F.A.C.G.

It is with deepest regret that we must accept the loss of Dr. Elihu Katz. He had originated and been associated with more worthwhile projects than anyone known to me. His expended energy towards completing these medical and other endeavors was boundless. Up to the very last moment he would have it no other way; he died at his office desk when he could have afforded, by all measures of right, to indulge himself in well-earned personal pleasures.

The helpful hand of Dr. Elihu Katz was always volunteered to students, colleagues, laymen, patients, institutions and organizations. His humor was

flavored with a genuine sincerity of friendship. All who knew Dr. Elihu Katz loved him.

He left valuable imprints too numerous to mention on the lives of thousands of people; many still unborn will benefit through his deeds. May his soul find the peace and tranquility that it justly deserves!

A. X. Rossien, M.D., F.A.C.G.

It was with a deep sense of personal loss that I learned of the death of a kind friend, Dr. Elihu Katz.

During my association with him I learned to respect him for his graciousness, sincerity and high ideals which won the genuine affection of his colleagues.

I extend my profound sympathy to the members of his family.

Samuel S. Berger, M.D., F.A.C.G.

The passing of our beloved Treasurer, Dr. Elihu Katz, on July 20, 1956, leaves a void in the ranks of the American College of Gastroenterology that can never be replaced. Elihu was a quiet, but a very sincere and loyal officer of this College. Whenever he spoke, he commanded instant attention and his remarks were always of importance and well considered. It was my great fortune to have known Dr. Katz for the past decade. I always had the greatest admiration for his superlative abilities, not only as an extremely skilled Treasurer of our College, but also as a sincere and staunch friend. I always looked forward with great anticipation to renewing my friendship with Elihu at the various meetings of the American College of Gastroenterology over the years.

My sincere sympathy is extended to the relatives of Dr. Katz in this period of their great loss.

Donald C. Collins, M.D., F.A.C.G.

To me it is a great satisfaction to remember as outstanding a physician as my good friend the late Elihu Katz. Perhaps the most pleasant memory occurred when the meeting of our College was in Los Angeles. In company with Dr. Katz and a close personal friend of his we toured not alone Los Angeles and San Francisco, but other places of interest. At the Farmer's Market we had dinner and later ascended the hill where many motion picture stars had their homes. I stress this because he introduced us to several of his friends all of whom had been his patients. His guardianship of the finances of our College were most interesting. I am convinced his friends will long cherish his memory.

H. M. Eberhard, M.D., F.A.C.G.

The untimely death of Dr. Elihu Katz has left a void in the lives of all who have had the privilege of knowing him and working with him. Despite prolonged illness he continued his activities with vigor and energy to the last. He truly died with his boots on as he undoubtedly desired.

The American College of Gastroenterology has lost one of its founding fathers and perennial treasurer, who has guided the organization through the lean years of the beginning to its present status of solvency by being a faithful watchdog of its finances. The College and all its members owe him a debt for his faithful services rendered to it.

To have known Dr. Katz, to have worked with him, to have conferred with him or to have conversed with him has always been a privilege and a delight. His cheerful disposition, attractive personality and intense interest in his chosen field of practice of medicine have left an indelible impression upon every one he came in contact with.

I, thus, publicly want to express my condolences and sympathy to the bereaved family of the late Dr. Elihu Katz.

I. R. Jankelson, M.D., F.A.C.G.

We were all saddened by the passing of our dear friend and fellow worker, Dr. Elihu Katz. His memory will remain with us as a staunch supporter of our College and one of the founders who never stinted his efforts in behalf of the organization that he was so proud of.

We shall always remember his tireless work as Treasurer, and even in the worst days of his severe illness, the progress and welfare of our College was always uppermost in his mind.

We shall miss him but he will always hold a cherished place in our memories.

Sigurd W. Johnsen, M.D., F.A.C.G.

I was one of the fortunate individuals who had the opportunity to know Dr. Katz. The esteem in which he was held by his associates and members of the Board of Trustees was pleasant to see. His service to the organization can never be replaced by any individual who would do a more thorough job. When Dr. Katz presented his reports everyone was at attention. Rarely ever were they questioned. As a physician and Man his patients and friends knew him as the epitomy of friendliness. It is with deep regret that we eulogize and therefore try to pay a small tribute to the late Elihu Katz.

S. Bernard Kaplan, M.D., F.A.C.G.

It is with great sorrow and heavy heart that I received the news of Dr. Elihu Katz being called to his eternal reward on July 20, 1956.

Dr. Katz was a man of high esteem, integrity, and principle in the field of gastroenterology, and beloved by all the members of the American College of Gastroenterology.

His advice and council was sought and accepted. His reasoning was sound, just, and fair, always keeping in mind the dignity of our college at all times.

In his capacity as treasurer of the college he served well—with honesty, and conscientiousness.

We of the American College of Gastroenterology will indeed feel the loss of Dr. Katz at our future meetings. A vacant chair shall be set aside with cherished memories of his attendances. Though he will not be with us physically I am sure his presence will ever be present and felt.

He will always be remembered for his outstanding ability as a gastroenterologist, for his unselfishness, for his courage, and for his convictions, and above all as a gentleman who commanded the respect of all of us at all times.

EDWARD J. KROL, M.D., F.A.C.G.

I mourn the loss of Dr. E. Katz. He was so modest, understanding, and kind, that I felt he was the impersonation of a truly great humanist. His interest in our Research Committee and his useful suggestions were of great help to me. His resignation in his fate, and yet his courage in facing it and the maintenance of a positive attitude to life, were truly great traits of this man. Please transmit my deep sympathy to his family.

H. NECHELES, M.D., F.A.C.G.

I have had the privilege of knowing Dr. Elihu Katz for more than one-quarter of a century, during which time I found him to be a fine gentleman, an outstanding gastroenterologist and a most devoted and loyal worker in the affairs of the College. His passing away has created an irreplaceable loss to the College, to his many colleagues and to the innumerable people he has helped in his most active professional career.

LOUIS L. PERKEL, M.D., F.A.C.G.

The death of Dr. Elihu Katz on July 20, 1956, was a great blow to many of his friends and patients, and also to the American College of Gastroenterology.

It had been my privilege to know Dr. Katz for many years, and to be associated with him at the New York Polyclinic Medical School and Hospital, where

Dr. Katz was an attending in gastroenterology. He was always very interested in the subject of gastroenterology, and spent a great deal of time in research and trying to improve his knowledge of the subject in which he was most interested. He has also been associated with the American College of Gastroenterology since its inception, and was a very loyal supporter.

His death is a severe loss to all of his friends and to those who had the privilege of being associated with him in his medical career.

WILLIAM B. RAWLS, M.D., F.A.C.G.

We noted with profound sorrow the passing of our esteemed colleague, Dr. Elihu Katz, on July 20, 1956. He died as he had always wanted to, namely, in his office, surrounded by the work which he had loved so well.

Dr. Katz was one of the original organizers of the National Gastroenterological Association. It was the inspiring efforts of that brave group of men that fostered the growth of our present College. He was tireless and devoted in his service to the Organization. For many years he served as its National Treasurer, giving unselfishly of his time and tremendous ability. When the original Association became the American College of Gastroenterology, Dr. Katz was one of the Charter Fellows. In addition to this work, he was affiliated with innumerable charitable institutions. He was a splendid teacher, leaving many fond memories amongst those of his students who are now practicing in different parts of the world.

We all miss him deeply.

CHARLES M. ROTHBURD, M.D., F.A.C.G.

It was with deep regret that I learned of the passing of Dr. Elihu Katz. During the many years that I was actively associated with the Executive of the National Gastroenterological Association, Dr. Katz was its Tresaurer. He took a great personal interest in the affairs of the Association and watched its finances during the many difficult years with marked efficiency. He was a loyal and true friend whose place will be most difficult to fill.

C. J. TIDMARSH, M.D., F.A.C.G.

The passing of Dr. Elihu Katz, to his eternal reward brought sadness to my heart. His zeal for the College, shown by his untiring work as Treasurer will long be remembered by the members of the Board—past and present.

F. H. VOSS, M.D., F.A.C.G.

For the second time in the space of six months, I sadly pen a tribute to a distinguished officer of the American College of Gastroenterology.

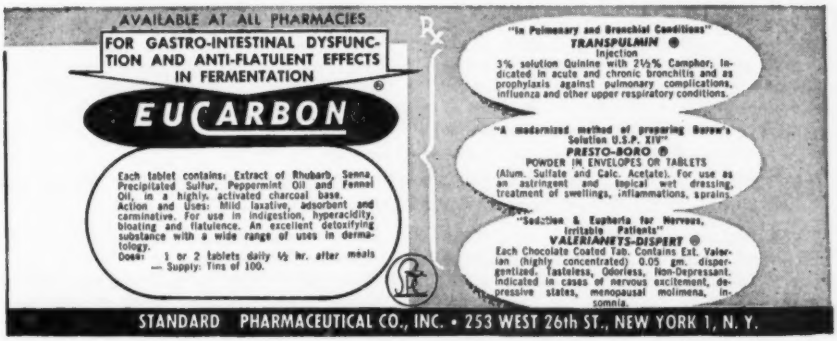
As Treasurer of the National Gastroenterological Association almost from its start and then of the American College of Gastroenterology, Dr. Elihu Katz served faithfully and well. His outstanding devotion to the College and his sincere desire to have it on a sound financial basis are in themselves a tribute.

In the many years in which I was associated with Dr. Katz in the work of the College, I always looked upon him as a friend and on innumerable occasions, his friendship to me was proven. Dr. Katz was a humanitarian and the word "no" was rarely heard when demands were made upon his time and his person for worthy causes, whether for individuals or organizations.

His sound advice on the financial affairs of the College were always a guide for me.

I will miss Dr. Katz greatly but will be the happier for having known this fine man.

DANIEL WEISS



ABSTRACTS FOR GASTROENTEROLOGISTS

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GASTROINTESTINAL TRACT

NEWER CONCEPTS OF DISEASES OF THE GASTROINTESTINAL TRACT: H. Necheles. Illinois M. J. 108:275 (Nov.), 1955.

Balance of food and electrolytes are greatly dependent on conditions within the digestive tract. Loss of potassium produces atony and distention of the bowel, while fluid loss carries with it alkaline salts thus tending to encourage "acidosis". In all conditions such as these, dehydration, of a serious nature, threatens.

Simpler sugars are rapidly absorbed and most fats emulsify in order to increase available surface for lipase to act upon. Some fats are not split and undergo absorption unchanged. Bile and pancreatic secretion are not essential for fat absorption. The quantity of fat in the stool increases after gastrointestinal surgery. Rapid dumping of food into the intestine is detrimental, as the small rhythmic spurts through the pylorus seems optimal for digestion.

After 60 years of age, the secretion of ptyalin is decreased, which interferes with starch digestion. Likewise, in the older group, gastric secretion decreases and to a lesser degree this prevails in respect to pancreatic lipase and trypsin. Added to lessened secretion is the factor of diminished absorption.

Normal tone and motility are necessary for optimal absorption. Decreased tone diminishes absorption. This introduces the question concerning the wisdom of exhibiting anticholinergic drugs in peptic ulcer.

REGINALD B. WEILER

GASEOUS INFLATION OF THE GASTROINTESTINAL TRACT: Milton M. Lieberthal and H. David Frank. New England J. Med. 253:901 (24 Nov.), 1955.

This article is in the nature of a brief discussion of the more common causes of gaseous inflation of the gastrointestinal tract. Two illustrative case reports follow the discussion. The accumulation of gas anywhere in the gastrointestinal tract represents the disparity at any given time between gas-forming and gas-removing mechanisms. Three possible means of gas accumulation are: 1. ingestion, 2. diffusion

from the blood stream, and 3. chemical change of intestinal contents. The first method accounts for about 70 per cent of the gas found in the gastrointestinal tract. Three possible means of gas escape are: 1. ejection, orally and/or rectally, 2. diffusion into the bloodstream, and 3. absorption through the intestinal wall. All the above methods are exclusive of experimental and therapeutic procedures. The two illustrated case reports demonstrate the complete filling of the gastrointestinal tract with air, in the absence of organic disease. The authors report that a perusal of the literature revealed reports of only six such cases.

CHESTER S. SVIGALS

BENIGN TUMORS OF THE STOMACH AND DUODENUM: THEIR RADIOLOGIC APPEARANCE: Robert N. Cooley and Vernie A. Stembridge. Texas J. Med. 51:754 (Nov.), 1955.

A total of 71 benign tumors of the stomach are reviewed. The most frequently benign gastric tumor is an adenomatous polyp; and the most common nonepithelial benign tumor is a leiomyoma. In the present series benign tumors of clinical or radiologic significance constitute about 3 per cent of all stomach tumors. In the material studied, there was scant evidence that benign mucosal polyps undergo malignant change. In only one case was a benign polyp found in the same stomach with a carcinoma. A review of 118 cases of carcinoma of the stomach seen during the past five years did not reveal a single case in which the tumor was thought to be a benign polyp by roentgen-ray examinations or gross inspection and then was found to be malignant on microscopic examination. Among 21 cases of pernicious anemia, adenomatous polyps of the stomach were found only once.

Benign tumors of the duodenum are less common than those of the stomach and are a rare cause of clinical symptoms. Only 1 of 9 tumors included in this series was of any clinical or radiologic significance. The roentgen-ray appearance of several benign tumors of the stomach and the duodenum is presented.

CHESTER S. SVIGALS

STOMACH

ORAL USE OF METHSCOPOLAMINE (PAMINE) BROMIDE IN TREATMENT OF DUODENAL ULCER: J. Alfred Rider, John O. Gibbs, William A. Ronson and Joyce I. Swader. J.A.M.A. 159:1085 (12 Nov.), 1955.

In this study 55 unselected patients with duodenal ulcer were used for clinical testing. Most of these had not done well on other ulcer routines and were considered to have chronic ulcers. Effects of usual clinical dosages of Pamine on basal gastric secretion were noted. The following conclusions were drawn: Pamine inhibits gastric secretion by decreasing both volume and free hydrochloric acid. The higher the initial level of free hydrochloric acid the larger the dose of Pamine required to induce anacidity. No diminution in the effect of single test doses of Pamine on gastric secretion was observed after prolonged administration of the drug. Sixty per cent of 55 patients with duodenal ulcer who received an average daily dose of 12.5 mg. complained of undesirable reactions. Most of these were mild. Pamine alone was seldom sufficient to completely relieve symptoms; results were usually better when antacids were added to the routine.

WM. K. BILLINGSLEY, JR.

GASTRIC BIOPSY WITH A MODIFIED AUSTRALIAN INSTRUMENT: N. F. Coghill and A. Wynn Williams. Brit. M. J. 4948:1111 (5 Nov.), 1955.

The search for a more acceptable instrument for gastric biopsy continues since the efforts of x-rays and gastroscopy, even when combined, cannot be relied upon at times.

The goals of any such instrument are: 1. to reach the area of the stomach to be biopsied, 2. to grasp a significant piece of tissue, 3. to avoid the dangers of hemorrhage, perforation or both from the procedure.

Despite the logical modifications made

in this Australian instrument, including a "stop", a screwable metal cap at the lower end of the tube and a concavity on the outside of the metal cap, the complication of hemorrhage was not obviated entirely. One of their patients died from uncontrollable bleeding following the procedure.

The authors feel, however, that except for general contraindications to gastric biopsy as in hemorrhagic disorders, congestive heart failure, portal hypertension and possibly severe anemias and old age (especially women), this instrument has been useful in their hands to elucidate the gastric histology in patients with dyspepsias and anemias of undetermined etiology.

A. M. SUSINNO

INTESTINES

ABNORMAL INTESTINAL DISTENTION AND CONTRACTION IN ACUTE ILEUS PART III: Shuhei Takita. Tokoshima J. Exper. Med., 2:20, (Jan.), 1955.

The authors performed experiments on cats and rabbits with specially devised abdominal windows. They recorded intestinal movements as well as internal pressure curve of a balloon just above an obstruction. It was noted that in the early stage of ileus the peristalsis and segmentation are more frequent, more vigorous and are larger as the intestinal contents increase. After 24 hours, due to venous congestion and intestinal distention each peristaltic or segmenting ring does not show complete relaxation, and the period of each rhythm is prolonged. Thus a continuous widespreading contraction of spastic type develops. This hypertonic state and the hypotonic state that follows are repeated alternately at long intervals. The pressure of the smooth muscle layer increases and causes orad transport of intestinal contents (fecal vomiting). The cause of intestinal distention in ileus is due mainly to gases and to some extent to stagnated food and increased intestinal secretions. In the later stages of ileus, meteorism near the obstruction is chiefly brought about by fermentation and putrefaction. Large bowel obstruction is prone to greater distention since here, even in the normal state, it contains a large amount of gas and feces. These gases cause distention by mechanical and chemical stimulation. Nitrogen, hydrogen, oxygen or air have no stimulating effect upon the movements. Carbon-dioxide, hydrogen disulphide, however, cause prolongation of peristaltic rhythm and periodic extreme relaxation (vicissitude type) of intestinal movement. Thus gases due to fermentation and putrefaction definitely influence the local dystonic state of the intestines in ileus.

A. J. BRENNER

PAINLESS PROCTOLOGY: Raymond L. Morrow. J. Missouri M. A., 52:705, (Sept.), 1955.

Painless examination is made possible, and painful lesions are soothed, by the use of a topical application of 1 per cent Tronothane solution or jelly. This surface anesthetic has no "caine" derivative, so that cross-sensitivity with other drugs is unlikely. It is quick acting, and aside from an occasional case of stinging, caused no side-effects over a 2-year period of study.

The author claims good results in fissures, and also (contrary to accepted opinion) in thrombosed external hemorrhoids and idiopathic pruritus ani.

NORMAN L. FREUND

ASSOCIATION OF GASTROINTESTINAL CARCINOID TUMOR WITH CARDIOVASCULAR ABNORMALITIES: David M. Spain. Am. J. Med., 19:366, (Sept.), 1955.

In order to further evaluate the incidence and pathogenesis of the syndrome of malignant intestinal carcinoid with hepatic metastases and fibrostenotic lesions primarily of the pulmonic and tricuspid valves, Spain reviewed 26 autopsied cases of carcinoid tumors derived from an autopsy series of 8,000 adults. These were compared with a control group of 500 autopsies sampled at random from the

entire series of 8,000 patients who were also studied relative to the presence of developmental cardiovascular defects and fibrostenotic lesions limited to the pulmonic and tricuspid valves. He demonstrated that carcinoid tumors of the gastrointestinal tract appeared to be associated with a high incidence of cardiovascular abnormalities. In addition to those cardiovascular developmental anomalies, acquired endocardial lesions predominantly involving the tricuspid and pulmonic valves are frequently present. The most advanced involvement of these valves is found in those cases in which the carcinoid tumor has metastasized. From the evidence presented, Spain feels that the syndrome is not merely a coincidence of conditions. The various theories advanced to explain this phenomenon are reviewed.

JOHN M. MCMAHON

WHIPPLE'S DISEASE: Robert H. Tuite and Henry Tesluk. Am. J. Med., 19:383, (Sept.), 1955.

To the total of 59 cases of Whipple's Disease reported in the literature, the authors add four cases diagnosed between 1943 and 1954. Case histories of brothers proved to have the disease and extensive history suggesting possible abnormalities in other members of the family are presented suggesting that a genetic mechanism may be of etiologic significance. It is felt that the primary defect is probably a metabolic one of the intestinal mucosal cell, resulting secondarily in a polyserositis as a result of hypersensitivity to a mucoprotein substance. Diagnosis by peripheral node biopsy is proposed. All three patients in whom microscopic examination of peripheral nodes was done, showed characteristic accumulations of Schiff positive macrophages, especially in the cortical areas. Pituitary adrenal factors have no fundamental role in the etiology or fatal outcome of the disease despite temporary improvement shown by some patients receiving ACTH or cortisone.

JOHN M. MCMAHON

CONGENITAL MALFORMATIONS OF THE RECTUM AND ANUS: Wallace M. Dennison. Glasgow M. J., 36:283, (Sept.), 1955.

The author reviews 34 cases treated since the advent of combined abdominal and perineal operation in the newly born baby. Up to 1949 the results of treatment were highly unsatisfactory.

The embryology and pathogenesis are briefly reviewed, and a classification into six types is given, rather than the four in common use. The two additional classifications are made to separate the rectovaginal and rectourinary fistulae in our type III cases.

The clinical features are described for each type. He stresses the waiting period of at least 15 hours, necessary to fill the hindgut with gas, before trying to interpret the x-rays taken in the inverted position. One case examined at 8 hours led to an unnecessary laparotomy, for the rectum was found only 1 cm. from the perineum.

The treatment is dependent upon the distance of the blind pouch of rectum from the perineum. If within 2 cm., perineal operation is performed; if above 2 cm., or when associated with vesical or urethral fistulae, a combined abdominoperineal approach is indicated.

The results are tabulated according to each type of deformity, and they bear proof of the excellence of our present method of treatment, and of the ability of the newly born to withstand major surgery.

NORMAN L. FREUND

ACUTE INTESTINAL OBSTRUCTION: Irving Rudman. Illinois M. J., 108:175, (Sept.), 1955.

The past 25 years has witnessed a shift of acute intestinal obstruction from the early postoperative period in young adults to very late postoperative or inoperative periods of the aged. This shift can be traced to the use of antibiotics pre- and

postoperatively combined with early ambulation, a therapy combination that prevents formation of abdominal adhesions.

Longer expectancy leads to an increase in abdominal neoplasms, which account for the great increase in the acute obstruction among the elderly.

For accurate diagnosis, x-ray interpretation should not be slavishly depended upon, for records indicate that 32 per cent errors were made in mechanical obstruction, 45 per cent error when gangrenous bowel was present, in small bowel obstructions, while 12 per cent error occurred in large bowel pathology.

The adage "when in doubt, operate", still holds good for accurate surgery.

J. EDWARD BROWN

MULTIPLE POLYPOSIS OF THE COLON: Frederick A. Coller and C. Thomas Flotte. J. Michigan M. Soc., 54:1061, (Sept.), 1955.

Multiple polyposis a rare familial disease is hereditary but not congenital. It generally appears at puberty and has a marked tendency to malignant change at an early age. The polyps are true adenomas and are present by the hundreds scattered from cecum to anus. They are most numerous in the flexures and sigmoid regions of the colon. They differ from acquired polyposis in being much more numerous and appearing at an early age and undergoing early malignant degeneration. There may be no signs or symptoms until malignant degeneration has taken place. More often, however, these patients complain of recurrent abdominal pain, cramps, bloody diarrhea, anemia, weakness and loss of weight. Occasionally partial obstruction or enlargement of a polyp or polyps in a localized area will call attention to the disease. Routine sigmoidoscopy may give rise to accidental discovery of this disease.

In a group of 63 patients operated on for this disease 59.2 per cent showed carcinomatous change. The average age of this group was 38.5 years, the youngest 13 years old.

The treatment recommended is total colectomy with establishment of a permanent ileostomy. If refused, subtotal colectomy with ileosigmoidostomy may be offered. In these patients the remaining colon should be able to be visualized by sigmoidoscopy and contain no malignant disease. The polyps present should be fulgurated and the patient appear for frequent examinations and fulgurations of recurrent polyps if present.

A. J. BRENNER

FAMILIAL POLYPOSIS OF THE COLON: William G. Whitaker and John E. Skandalakis. J. M. A. Georgia, 44:448, (Sept.), 1955.

Familial polyposis of the colon has frequently been misnamed congenital polyposis, an error in judgment, since no case of colonic polyps has been demonstrated in very young children.

It is a disease of youth and early middle age, transmitted from parents by gene mutations that adhere closely to Mendel's Law, deviating only in the ability to be dominant or recessive, thereby producing the condition in succeeding generations or skipping generations when recessive, to reappear when both parents have the recessive gene.

The polyps themselves are elongated protrusions of the colonic mucosa, on stalk-like pedicles with connective tissue hyperplasia in the bodies, this hyperplasia being the progenitor of the malignancy that occurs in practically all of the cases.

The diagnosis is simple: a history of rectal bleeding with mucus diarrhea and a gradually increasing anemia. As most of the polyps are in the sigmoid and rectum, an ordinary rectal digital will reveal their presence. This should be followed by a complete sigmoidoscopic inspection.

Treatment consists of surgical removal of the entire colon including rectum with formation of a permanent ileostomy or total colectomy with ileorectostomy, followed by actual cautery fulguration of all polyps in the rectal segment.

Close follow-up examinations are necessary in the second choice operation to obviate neoplastic degeneration.

J. EDWARD BROWN

TRUE ENTEROLITHS OF THE SMALL INTESTINE: F. S. Fowweather. Brit. M. J., 4946:1010, (22 Oct.), 1955.

This paper presents three cases of true enteroliths of the small bowel, going in detail into the size and composition of the various stones. In general, they are composed mainly of bile acids, or of calcium oxalate, of phosphate.

The clinical data is omitted, but may be presented at a later date. The author goes into the mechanism of the formation of stones, and shows that many have started with a nidus of fruit stone.

CORTISONE IN ULCERATIVE COLITIS: S. C. Truelove and L. J. Witts. Brit. M. J., 4947:1041, (29 Oct.), 1955.

This is a long paper giving the final report on the results of treatment of 210 patients with cortisone or a blank tablet as a control. One hundred nine received cortisone, and 101 the blank tablet. The dosage, for the most part was 100 mg. per day. The group receiving cortisone showed much better results in both categories than the control group. The authors also show the effect of treatment in relation to the severity of the initial attack, and it is here that the most dramatic results are obtained, indicating that in very severe cases, those who received cortisone did very much better than the control group. There were 16 deaths in this group: 5 in the cortisone group, and 11 in the control group.

Long term results: 205 of the 210 were able to be followed at the end of nine months. Those who were classified as "first attack" showed a much greater degree of improvement over the control group. In the groups classified as "relapses", however, the control group did as well as those on cortisone, except that there were a few more deaths in the control group. Those who remained alive, however, were about as well off as those in the cortisone group. In this period, nine more died.

The evidence is certainly in favor of the group receiving cortisone.

DILEMMA OF THE RELAXED INGUINAL RING: M. S. DeWeese and Daniel C. Hunter, Jr. J. Michigan M. Soc., 54:1214, (Oct.), 1955.

The authors point out that the anatomical variant: relaxed external inguinal ring is responsible for a high percentage of hernia surgery. They feel that only by coordinated study and effort, medical, industrial and military, can such unnecessary operations be curtailed.

In a small group, who are refused employment because of inguinal canal abnormalities unless repaired, only 53.5 per cent were found to have true herniae. The authors believe that there are entirely too many employment rejections based on the erroneous conception that relaxation of the external inguinal ring contributes to the subsequent development of hernia. Unfortunately, as they point out, the factual statistical data is sparse.

IRVIN DEUTSCH

STEATORRHEA: A REVIEW OF 40 PATIENTS, WITH PARTICULAR REFERENCE TO DIAGNOSIS: P. H. Friedlander. Brit. M. J., 4943:809, (1 Oct.), 1955.

The differential diagnosis of the cause of steatorrhea is of primary importance insofar as the treatment of the condition is concerned, for in certain cases of secondary steatorrhea surgical treatment may be curative. In cases of secondary steatorrhea with some clinically obvious mechanism of disease process, as in chronic obstructive jaundice, the treatment is that of the primary disease and not of the steatorrhea, which is merely a symptom; moreover, the differential diagnosis of such conditions from idiopathic steatorrhea is not difficult.

However, those cases of secondary steatorrhea with a clinical picture similar to that of idiopathic steatorrhea, such as the postoperative blind-loop syndrome or pancreatitis, must clearly be differentiated from

this condition. Idiopathic steatorrhea often presents a definite clinical picture, the correct diagnosis being suggested on these grounds alone. Thus steatorrhea in a patient who is otherwise fit and well nourished is more suggestive of chronic pancreatitis than of idiopathic steatorrhea. Previous history of abdominal operations, a history of childhood diarrhea, the presence of a small-bowel lesion on barium-meal examination and tests of pancreatic function may also be useful.

Finally, if there is still some doubt about the etiology, together with a reasonable chance of a correct diagnosis leading to a successful treatment, a laparotomy should be considered.

ALEXANDER ZABIN

STEATORRHEA: A. C. Frazer. Brit. M. J., 4943:805, (1 Oct.), 1955.

Steatorrhea is taken to mean the passage of loose, bulky, pale, fatty, offensive stools. The steatorrheic stool has an increased water content, increased dry weight, normal amount of pigment, which is paler than usual, increased amount of long-chain fatty acids, and increased short chain volatile fatty acids. The long-chain fatty acids may be of dietary or nondietary origin, or both. The nondietary fat may be excreted, or it may be synthesized in the intestine. Increased activity of intestinal organisms may play an important part in the stool changes. Steatorrhea is, usually, secondary to defective intestinal absorption. "Idiopathic steatorrhea" can now be classified into the pancreatogenous, hepatogenous, and enterogenous groups. The last named can be further differentiated into gluten-induced enteropathy, tropical sprue, or one of the anastomotic syndromes. The dietary regime is planned to reduce bacterial activity in the intestine. Specific measures in appropriate cases include replacement of pancreatic enzymes or bile salts, a gluten-free diet, folic acid therapy in early sprue, antibacterial therapy in more chronic cases and corrective surgery. Cortisone is helpful in some cases of idiopathic steatorrhea.

ALEXANDER ZABIN

THREE AND FIVE-YEAR SURVIVALS FOLLOWING COMBINED ABDOMINO-PERINEAL RESECTION. ABDOMINOPERINEAL RESECTION WITH SPHINCTER PRESERVATION, AND ANTERIOR RESECTION FOR CARCINOMA OF THE RECTUM AND LOWER PART OF THE SIGMOID COLON: John M. Waugh, Melvin A. Block and Robert P. Gage. Ann. Surg., 142:752-757, (Oct.), 1955.

The authors compared three-year and five-year survival rates for each of the three procedures:

a. Combined abdominoperineal resection.

b. Combined abdominoperineal resection, with preservation of the external sphincter.

c. Anterior resection with primary anastomosis.

In addition to this, they submitted a break-down, based on the level of the lesion, from the anal orifice. It included a total of 625 cases from the years 1941 to 1950. The results were submitted in table form. Of these, 444 cases fell into the three operative procedures, and an overall mortality rate of 3.8 per cent is reported. Three and nine-tenths per cent for the anterior resection, 3 per cent for each of the two other procedures. The authors' policy since 1945 has been to restrict the combined abdominoperineal resection to lesions located from 0 to 5 cm. from the anus. For lesions 6 to 10 cm., the sphincter preserving operation has been used as much as technically possible. They state that insofar as five-year survival is concerned, the Miles operation does not appear to have any advantage over the so-called more conservative procedures.

A similar table is submitted for three-year survival rates.

PAUL MATLIN

THE MEDICAL MANAGEMENT OF ULCERATIVE COLITIS: Alice Lowell. Am. J. Proct., 6:377, (Oct.), 1955.

The physician treating ulcerative colitis is at once handicapped because he knows neither the cause or cure, nor can he prevent complications. The complications

which are not specifically part of the disease but are abnormalities of structure and function are dehydration, electrolyte imbalance, ischemic nephrosis, renal calculi, amyloid disease, fatty liver, bowel hemorrhage, perforation, and sepsis. There are also complications such as arthritis, keratitis, pancreatitis, pustular or necrotizing skin lesions, and erythema nodosum, possibly manifestations of a widespread systemic disease of which the colon lesions are only a part.

The patient, when presenting himself for treatment must be managed first, as a human being: emotional problems, conflicts, anxieties, etc., to be understood, and resolved. Secondly, as a sick person, bed rest and complete medical survey must be made. Thirdly, his fever creates metabolic disorders, and dehydration. Fourthly, because of the diarrhea, food loss, vitamin blood, mineral (especially sodium, chloride and potassium) loss, aided by anorexia, are serious problems to be anticipated.

These lead to alkali, protein and vitamin deficits, an impending acidosis which, early, can be compensated by kidney function. Thus, early evaluation of renal function must be made, and supported, for a later renal impairment seriously hampers correction of the many metabolic and mineral changes. The renal function status influences the interpretation of the hematocrit, protein levels, and mineral values especially potassium.

Fluid replacement may of necessity be much greater than usual fluid requirements, depending on extent of diarrhea. Hypotonic fluids are best, early, and blood transfusions should be used freely. The Machella diet of frequent high protein, high caloric, low residue mixtures is best. Parenteral feedings may be necessary. Vitamins, antispasmodics, and sedatives are used. The steroids are valuable to induce remissions. Sulfonamides and antibiotics are best reserved for situations in which sepsis or peritonitis is present.

In spite of remissions, the internist is faced with the fact that the patient still has ulcerative colitis, and that exacerbations, perforation, malignancy, and other conditions may still occur.

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MANAGEMENT OF LESIONS OF THE COMMON DUCT: Joseph A. Soffel. Pennsylvania M. J., 58:1108 (Oct.), 1955.

"The prevention of lesions of the common duct begins with the proper management of the original disease of the gallbladder and consists in careful and safe technic in the removal thereof. . . . Repair of injury to the common duct prevents many difficulties which increase with each subsequent repair. The first operation has the best chance of success and should be done meticulously".

These are the basic themes expanded upon by Dr. Soffel as he enumerates in detail the pitfalls in surgical technics leading to common duct lesions. The general surgeon can profit greatly by reading this excellent summary.

However, the gastroenterologist, the internist and the general practitioner may not be in full accord with the indications listed for doing cholecystectomies in the first place.

Exception would certainly be taken to the dictum that "acute cholecystitis which does not subside should have an operation within the first 48 hours" or that an indication for cholecystectomy is "one or more attacks of acute cholecystitis".

With few exceptions the one definite indication for cholecystectomy is the visualization of stones by x-ray. But even here it is not certain whether this should be a hard and fast rule in the aged or poor risk patient or even in the asymtomatic young patient.

Since the careful and detailed discipline for doing cholecystectomies is not always followed, infarct sometimes avoided, an important contribution to fewer common duct problems would be to undertake fewer cholecystectomies except for strict indication, avoiding the operation in the acute phase if possible.

A. M. SUSINNO

BOOK REVIEWS FOR GASTROENTEROLOGISTS

THE BODY FLUIDS—BASIC PHYSIOLOGY AND PRACTICAL THERAPEUTICS: J. Russel Elkinton, M.D., Associate Professor of Medicine, Chief of the Clinical Section of the Department of Medicine, University of Pennsylvania School of Medicine, etc., and T. S. Danowski, M.D., Renziehausen Professor of Medicine, Senior Staff Physician at the Children's Presbyterian Women's Hospital, etc., University of Pittsburgh School of Medicine. 626 pages. The Williams & Wilkins Co., Baltimore, Md., 1955. Price $10.00

Numerous volumes have appeared recently devoted to the Body Fluids, their electrolyte composition in health and disease. The increased need for basic understanding of the physiology and pathology of body water and electrolytes for a successful program is well documented in this volume. The therapy of excesses of water or of the chief electrolytes, sodium and potassium, is comprehensively discussed in Chapter 9—page 214. The use of cation exchange resins, the artificial kidney, etc., are some of the important topics the reader will find both interesting and applicable in therapy. Diabetic ketosis and coma; losses of water, sodium, potassium, etc., in diabetic acidosis and coma and the blood serum solutes and electrolytes, prior to therapy, and many other pertinent facts, are found throughout the pages.

On page 414, the reader will find valuable hints on hypo- and hyperfunction of the adrenal cortex. The effect of cortisone therapy on adrenal cortical hypofunction—page 421, tumors or hyperplasia (Cushing's syndrome), the prevention or cancellation of toxic or side-effects of ACTH or cortisone therapy, are worthwhile facts to be read by the practitioner.

Sample diets, extensive references and cross index makes this monograph an outstanding and useful addition to the already overfilled physician's library.

1955-56 YEAR BOOK OF MEDICINE: Edited by Paul B. Benson, M.D., Carl Muschenheim, M.D., William B. Castle, M.D., Tinsley R. Harrison, M.D., Franz J. Ingelfinger, M.D. and Philip K. Bondy, M.D. 711 pages, illustrated. The Year Book Publishers, Inc., Chicago, Ill., 1955. Price $6.00.

As usual, the volume is divided into chapters dealing with infections, the chest, the blood and blood forming organs, the heart, the blood vessels and kidneys, the digestive system and metabolism. In each of these sections, a careful selection has been made of the world's medical literature and abstracted in readable form, so that the physician may familiarize himself with what is new in diagnosis and treatment in the medical field.

An extensive author's index and cross-references complete this practical volume.

1955-56 YEAR BOOK OF GENERAL SURGERY: Edited by Evarts A. Graham, A.B., M.D., with a section on Anesthesia, edited by Stuart C. Cullen, M.D. 655 pages, illustrated. The Year Book Publishers, Inc., Chicago, Ill., 1955. Price $6.00.

Surgeons will find the Year Book of General Surgery very useful in their practice, whether general or special surgery is their field. Like all year books, in this volume, abstracts of the world's surgical literature bring newer and advanced methods to the attention of the surgeon. It is a very practical text and is highly recommended.

CHIRURGIE DE LA RATE: Jean Patel, Adjunct Professor of the Faculty of Medicine, Paris, Surgeon, Hospital Tenon. 387 pages, illustrated. Masson et Cie, Paris, France, 1955. Price 3,400 fr.

A beautifully printed and illustrated volume dealing with operations on the spleen. Numerous illustrations are reproduced from J. Auvert and L. Leger, which enhance the value of the book. On page 228, an excellent x-ray finding is shown of varices of the

esophagus found in portal hypertension. page 256, the author describes a method of tamponing the esophagus by means of the Blakemore and Senstagen balloon.

Although there is lack of extensive American references, this does not detract from the usefulness of the book.

PROBLEMS IN AMEBIASIS: Charles William Rees, Ph.D., Head, Section on Protozoal Diseases, Laboratory of Tropical Diseases, National Microbiological Institute. An added chapter—Clinical Notes on the Etiology, Pathology, Clinical Management and Therapy of Amebiasis: Clarence A. Imboden, Jr., M.D. 119 pages, illustrated. Charles C. Thomas, Springfield, Ill., 1955. Price $4.75.

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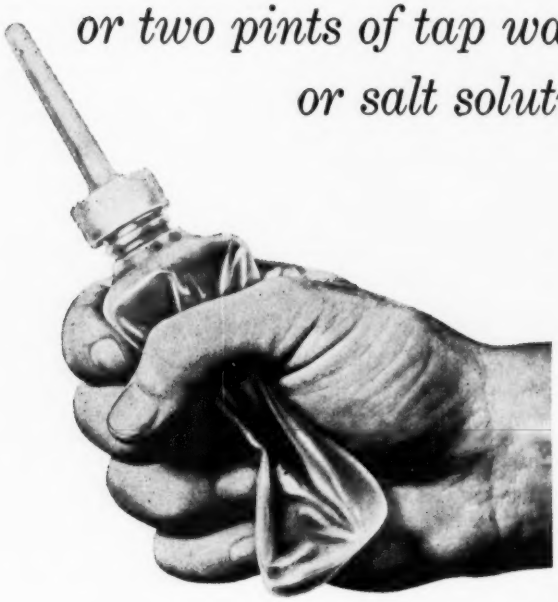
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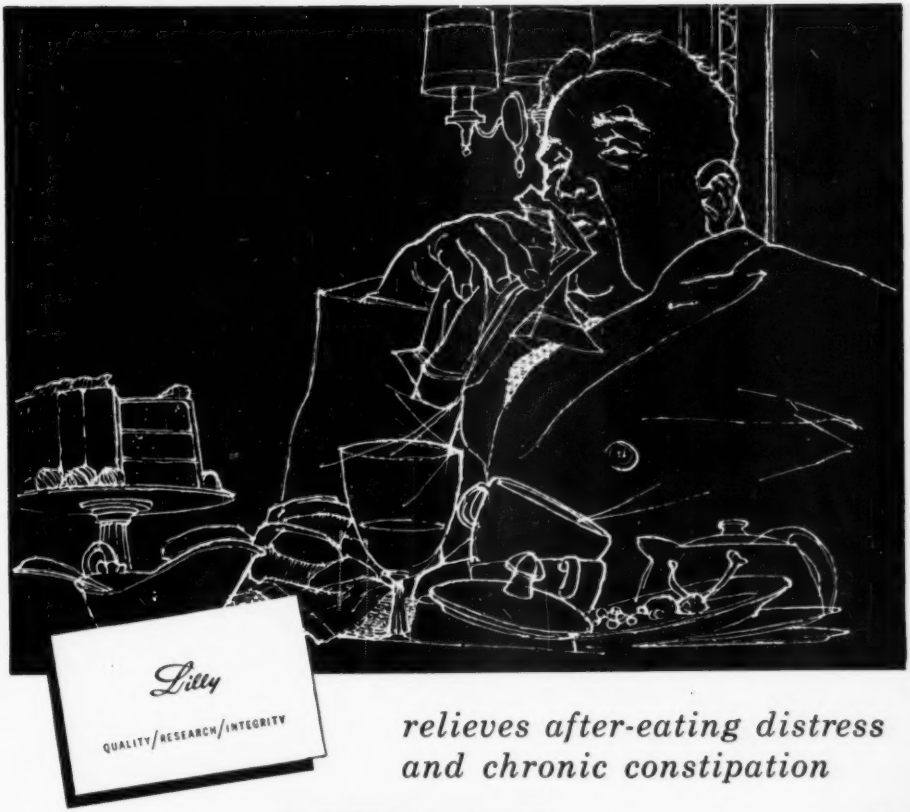
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2. Morrison, Samuel: Am. J. Gastroenterology 22:309 (1954).
3. Rossett, N. E., Rice, M. L., Jr., Gastroenterology 26:490 (1954).

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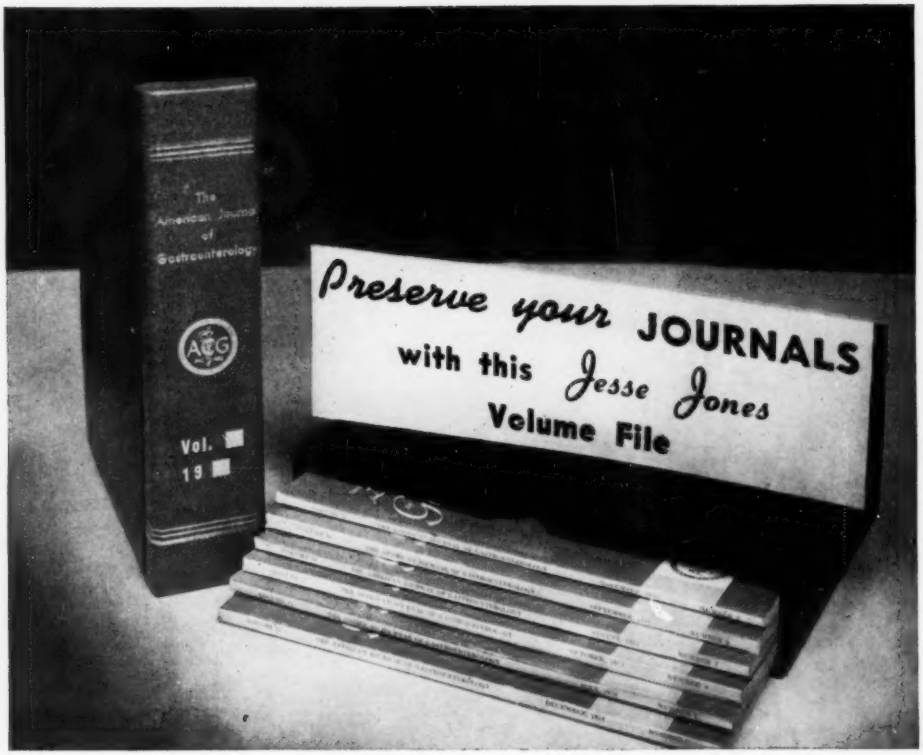
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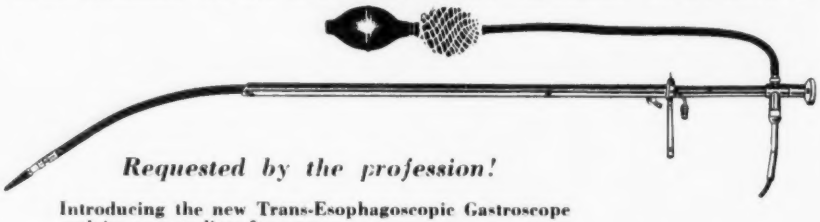
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1. Watt, B.K., and Merrill, A.L.: Composition of Foods—Raw, Processed, Prepared—Washington, D.C., United States Department of Agriculture, Agricultural Handbook No. 8, 1950.

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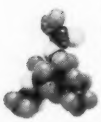
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